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VOLUME XXXV • NUMBER 2
FEBRUARY 1959

DISEASES of the CHEST

OFFICIAL PUBLICATION

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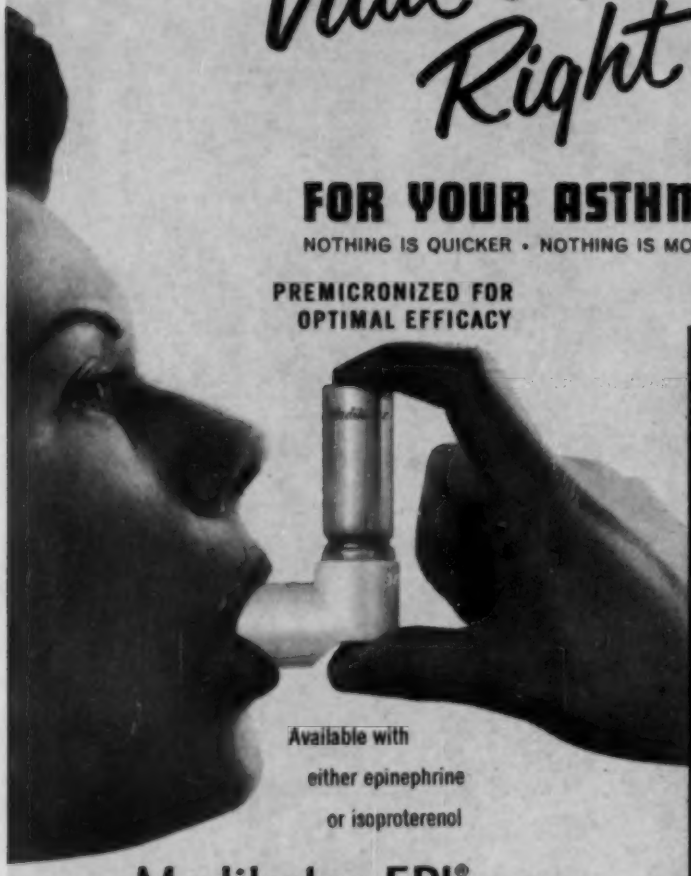

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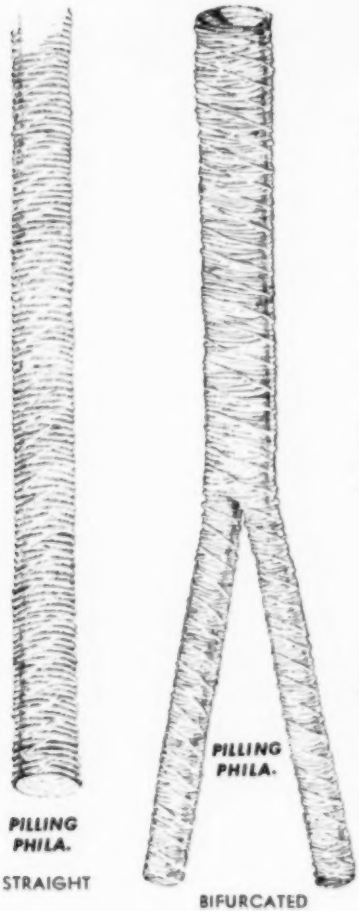

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1. DeBakey, M. E., Cooley, D. A., Morris, G. C., Jr., Collins, H.: Arteriovenous Fistula Involving the Abdominal Aorta. Annals of Surgery, 147:646 (May, 1958).

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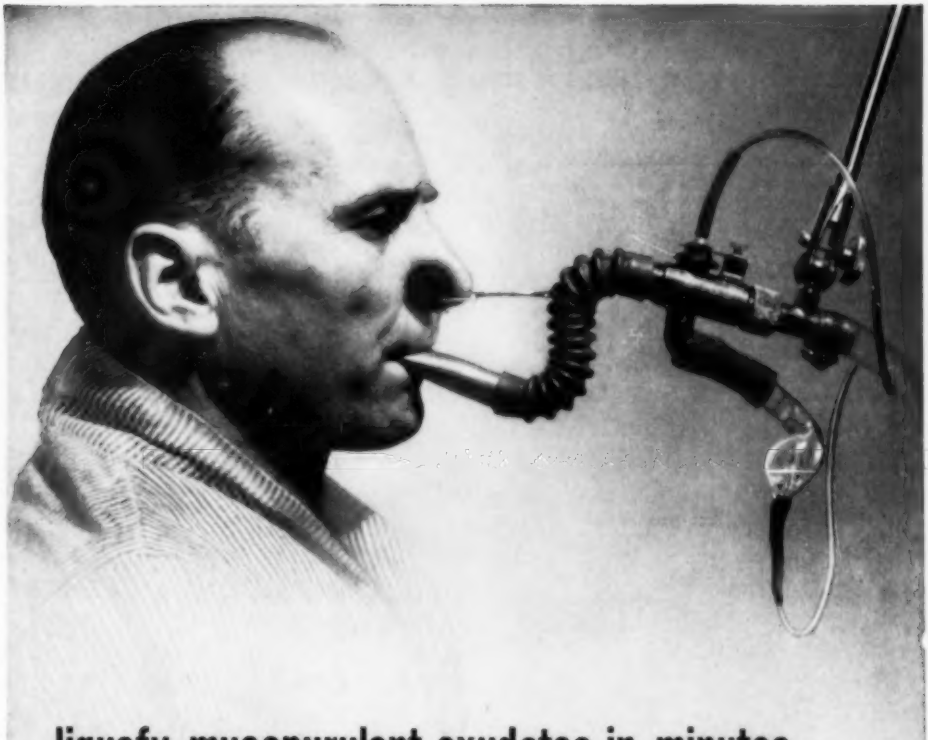

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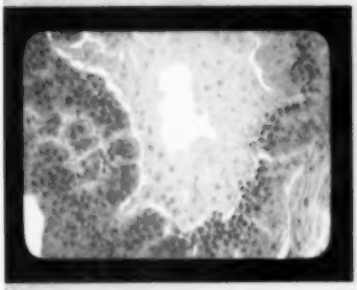

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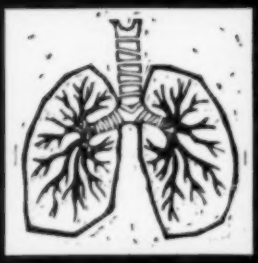

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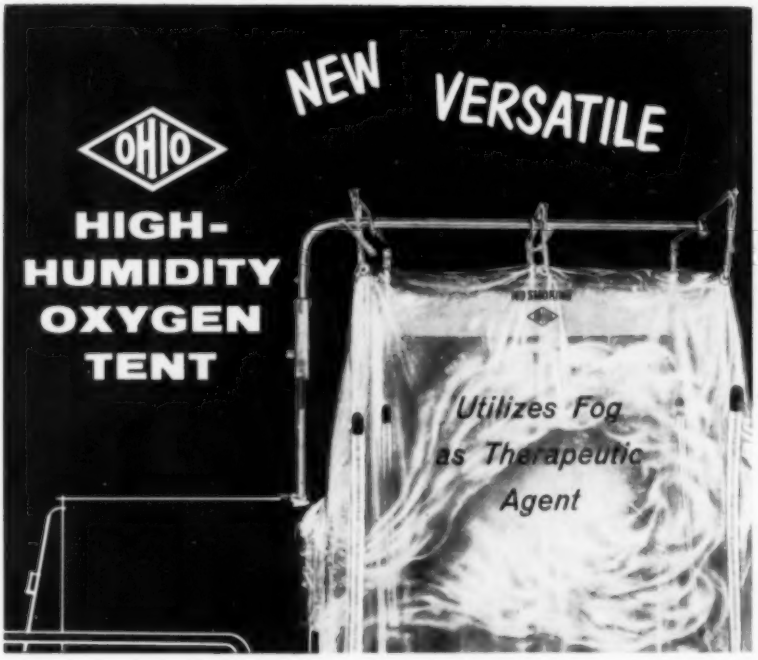

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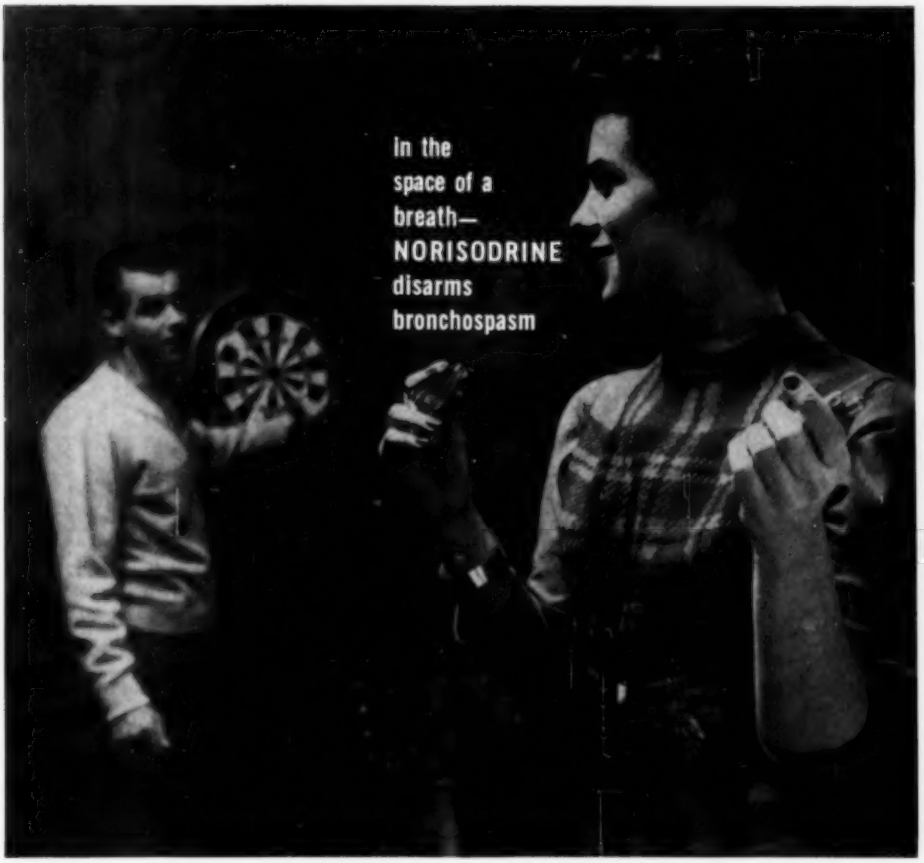

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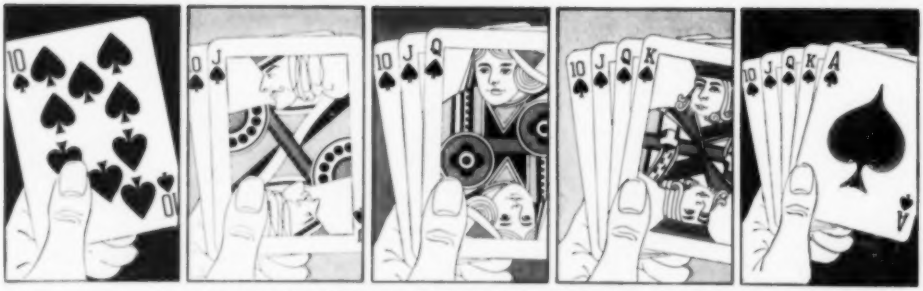

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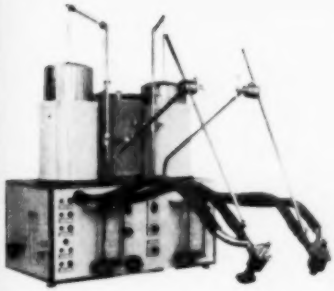

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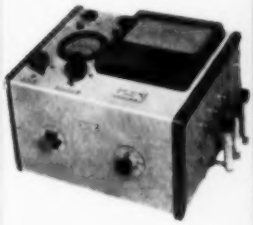

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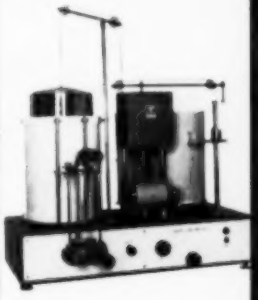

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4. TESSALON increases vital capacity and ventilation.
5. TESSALON improves exercise tolerance.
6. TESSALON relieves dyspnea.

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Cough suppressing activity of TESSALON[3]

	Average Number of Coughs*
No therapy	8.3
Codeine	4.4
TESSALON	1.7

*Based on 5-minute interval immediately following inhalation of citric acid to induce cough. Each patient was tested on three separate occasions.

Controls cough in the chest

It has been shown that the increased sensitivity of the sensory receptors in the lung during inspiration is an important part of the cough mechanism. TESSALON has a selective inhibiting effect on these dilation or "stretch" receptors[4] that helps to control cough where cough begins—at points of irritation in the chest.

Controls cough at the cough center in the medulla

Spinal reflex arcs were studied for the inhibitory effect of TESSALON on the transfer of afferent cough impulses to the efferent branch of the cough reflex.[5] The administration of TESSALON inhibited reflex transmission, when the afferent nerve was stimulated electrically. With this "damping" effect on the cough center in the medulla, TESSALON controls cough centrally, as well as peripherally.

Thins sputum

TESSALON controls cough frequency without interfering with productivity or expectoration. In fact, sputum is usually thinner, easier to raise.[1]

Effect of TESSALON on sputum[1]

Amount		Consistency	
Less	32 patients	Heavier	3 patients
More	2* patients	Lighter	27 patients
Same	16 patients	Same	20 patients

*These patients noted more but lighter sputum.

Increases vital capacity

Respiration usually increases both in depth and volume during TESSALON treatment.[6] In one study,[7] patients with chronic respiratory disease, with and without bronchospasm, showed a mean increase of 19.7 per cent in vital capacity after a 2-week course of TESSALON.

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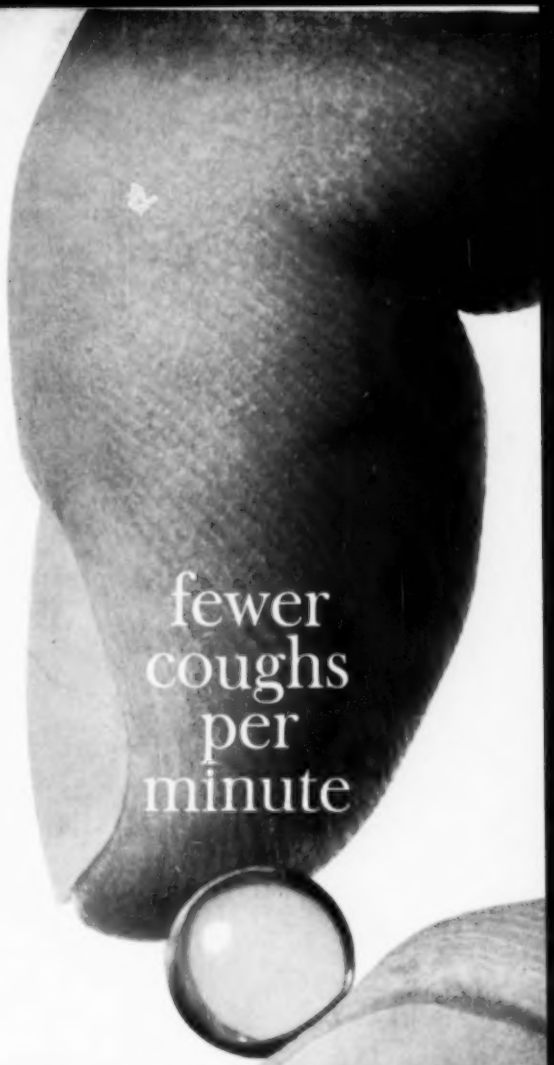

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PROCEDURES: Bronchoscopy and bronchography, Thoracentesis, Thoracic surgery

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ADULTS: Average dosage is one Perle (100 mg.) t.i.d. If necessary, or where cough is refractory, up to 6 Perles (600 mg.) daily may be given.

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The Perles should be swallowed without chewing, and, if necessary, with a liquid. Release of TESSALON from the Perle in the mouth produces a temporary local anesthesia of the oral mucosa.

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TESSALON is well tolerated. Only occasionally have side effects been reported. Skin rash, nasal congestion and a vague "chilly" sensation have been mentioned. In rare instances, gastrointestinal upset, constipation or sedation have been observed. No adverse effects on respiration, kidney or liver function tests, blood count or urinalysis were reported.

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References

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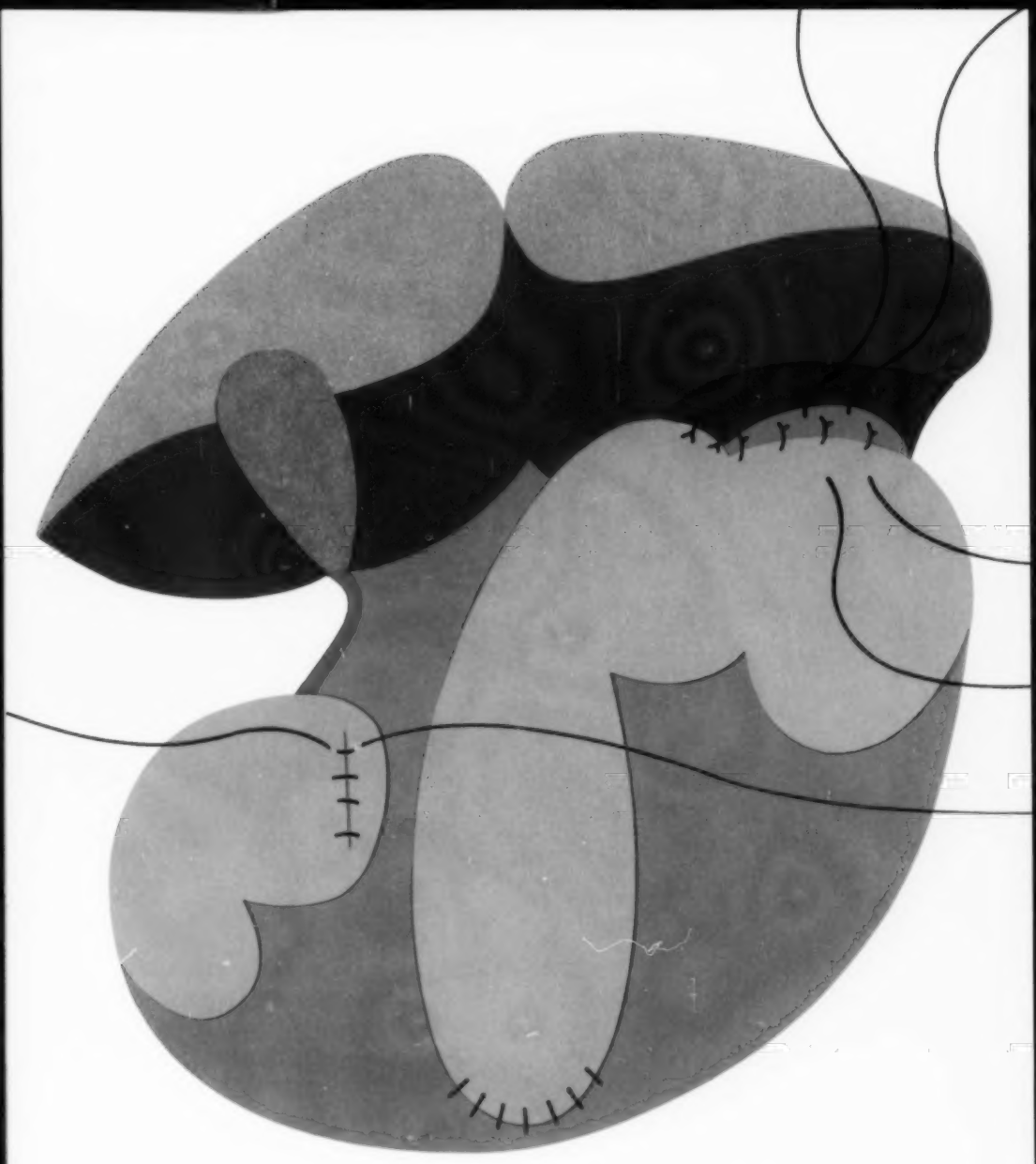

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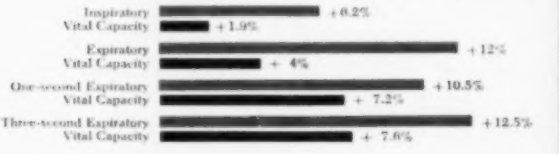

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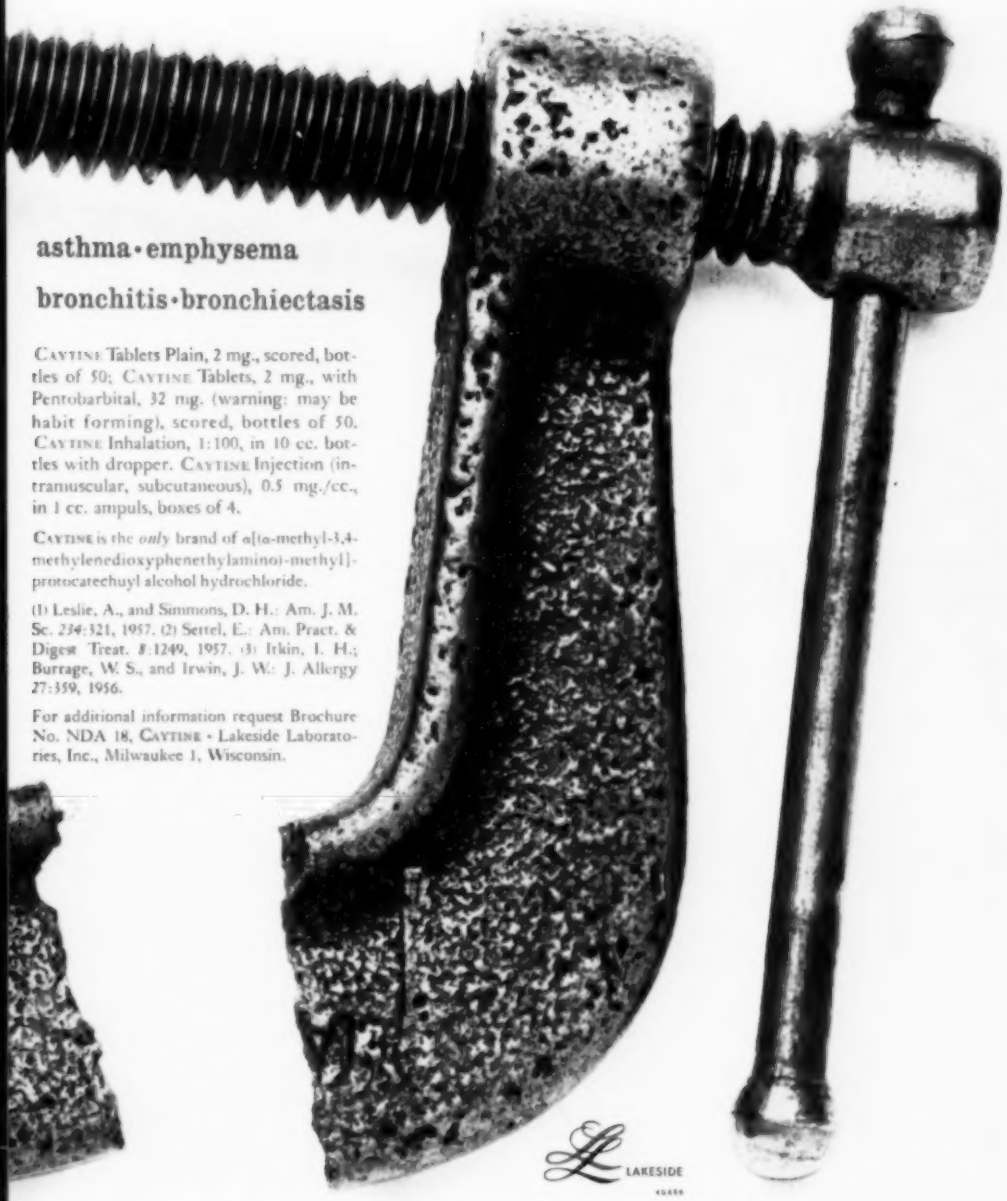

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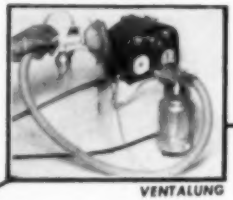

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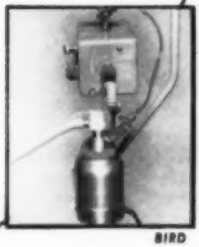

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*Silbert, N. E.: Dis. Chest 29:520, 1956.

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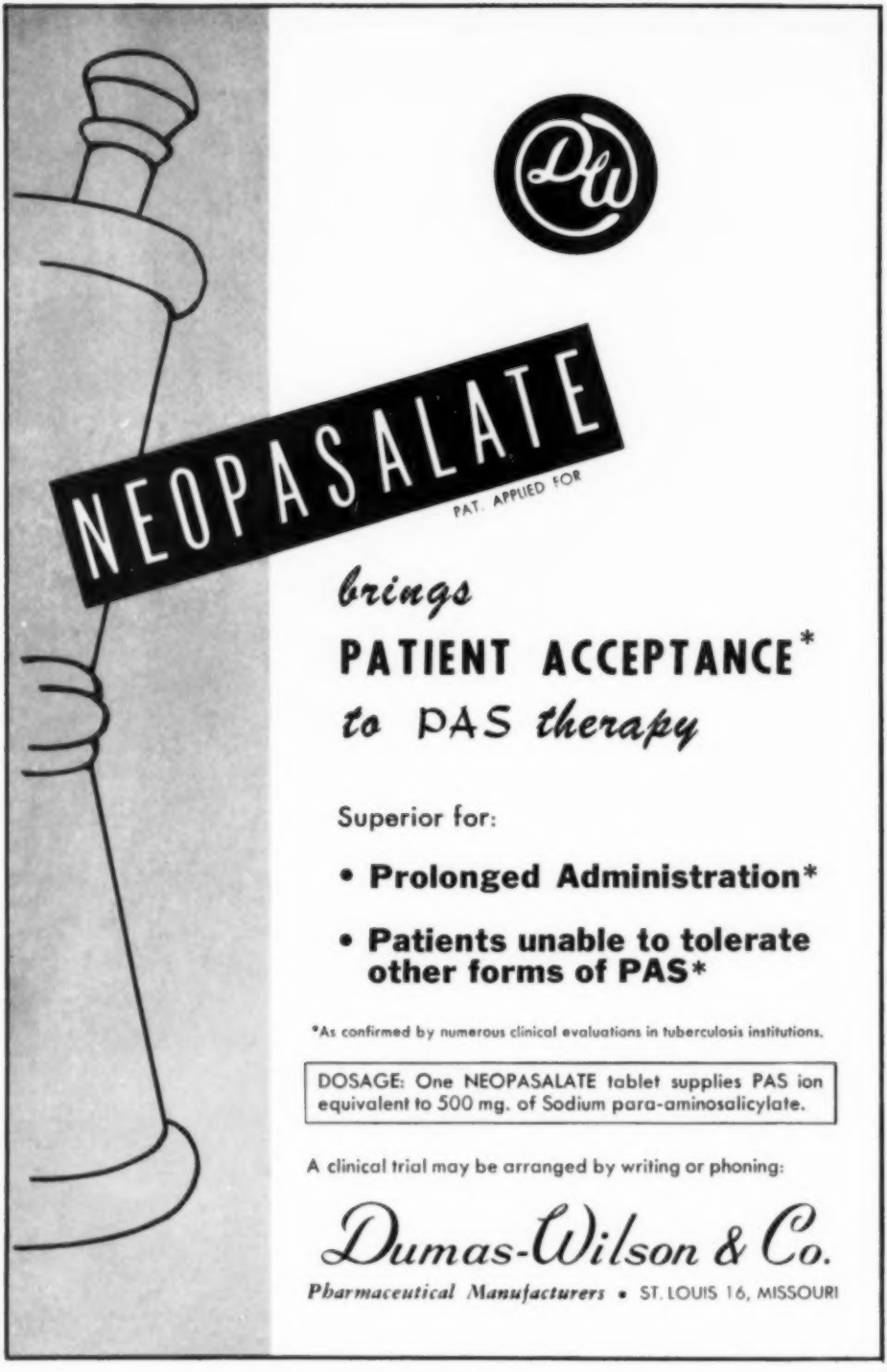
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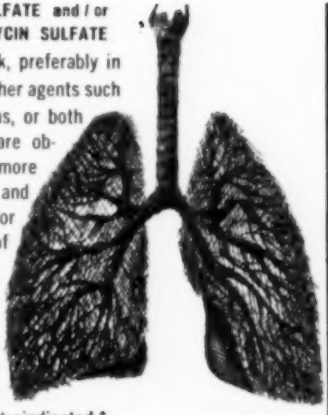

*Committee on Chemotherapy and Antibiotics, American College of Chest Physicians. Present status of chemotherapy in tuberculosis, J. Indiana M. A. 51:799 (June) 1958

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References:

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DISEASES of the CHEST

VOLUME XXXV FEBRUARY, 1959 NUMBER 2

Fluoroscopic Pulmonary Densiography*

ALBERT H. ANDREWS, JR., M.D., F.C.C.P.,[1] ROBERT JENSIK, M.D., F.C.C.P.[2] and WILLIAM H. PFISTERER, M.D.[3]

Chicago, Illinois

Kourilsky and Marchal[1] presented papers at the Fourth International Congress on Disease of the Chest which stated an accuracy of 90 and 95 per cent in the diagnosis of bronchogenic carcinoma by their technique of fluoroscopic densiography. They have also reported on the use of their methods as a means of differential pulmonary function study.[2] This study was undertaken because their methods appeared to offer promise of recognition of localized pulmonary disease and areas of localized dysfunction.

Method

A photomultiplier tube with a sodium iodide crystal is exposed to the fluoroscopic beam after passage through the chest by means of an orifice 3/32 inch in diameter and 1/8 inch long. The system is centered on the x-ray tube and mounted on the patient side of the fluoroscopic screen. The output of the tube is filtered, the impedances matched, and recorded photographically by a mirror galvanometer. Improvements in the circuitry are being made so that presentation of details will be made at an appropriate stage in the work (Fig. 1).

The direct current output is measured by a damped vacuum tube voltmeter both with and without the patient. The fluoroscopic density is the percentage drop in voltage between the output with and without the patient. The variation in the output is recorded as an indication of the volume change of the chest due to respiration.

The fluoroscope is adjusted to 80 kilovolts and 1.5 milliamperes which delivers 1.5 roentgens per minute at the table top.

*With the technical assistance of Webster E. Gilman, B.S., I.R.E.
From the Respiration Laboratory and Department of Roentgenology, Presbyterian-St. Luke's Hospital, St. Luke's Division.

[1]Attending Broncho-esophagologist and Director, Respiration Laboratory.

[2]Attending Surgeon.

[3]Attending Radiologist and Acting Chairman, Department of Roentgenology.

Assisted by Grants from: American College of Chest Physicians, Council on Research; American Medical Association, Council on Physical Medicine and Rehabilitation; Linde Company.

Acknowledgments: Edward L. Jenkinson, M.D., Consulting Roentgenologist; Standard X-ray Corporation, Chicago, Illinois; Radio Corporation of America, Tube Division, Lancaster, Pennsylvania; Nuclear-Chicago Corporation, Chicago, Illinois.

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The orifice is usually placed over three areas on each side. Each area is approximately two-thirds of the distance between the spine and the lateral chest wall. The areas are subclavicular, opposite the hilus, and one interspace above the diaphragm at the end of expiration. The orifice is always placed over an anterior intercostal space and, whenever feasible, over a posterior interspace. The shutters are adjusted to expose an area about two inches square. The duration of x-ray exposure is indicated by a timer. The usual examination requires about 10 minutes, or a total exposure of about 15 roentgens. Patients in the child bearing age group are given further protection by lead shielding below the diaphragms.

Calibration circuits with corrections for filters and breathing rate permit voltage measurements of the respiratory fluctuations. These fluctuations are expressed as a percentage of the output over each area. The fluctuations of one area are expressed as a percentage of the sum of the fluctuations over one side and give an estimation of the ventilation in the

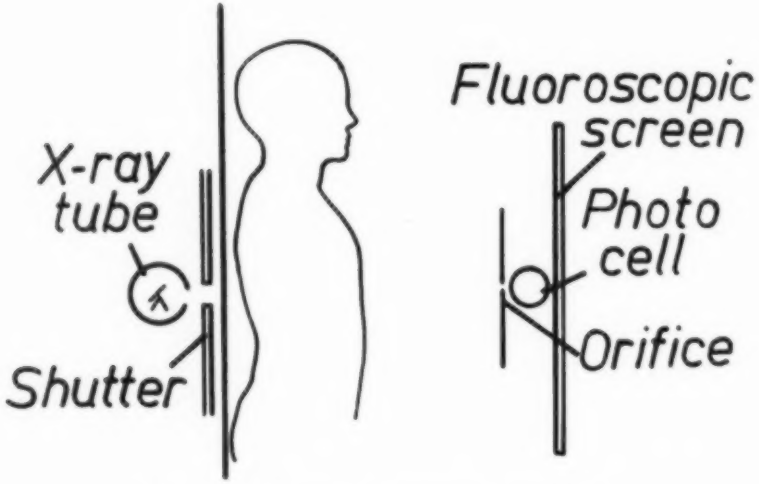

FIGURE 1: Diagram of fluoroscopic densiograph.

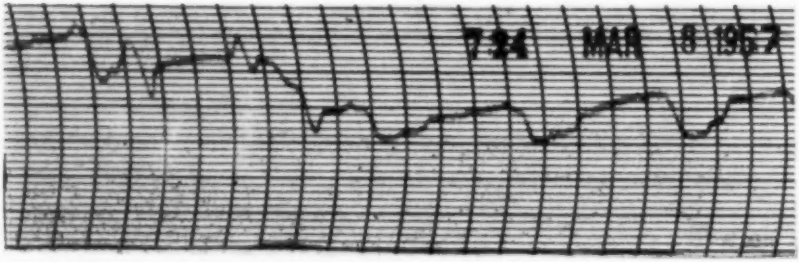

FIGURE 2: Male, 47 years. Bilateral pulmonary cysts and blebs. Area: left upper lung. Progressive inflation and reduction of respiratory excursions during forced respiration made an additional diagnosis of pressure cyst which was confirmed at thoracotomy.

area as compared to the total for that lung. The total fluctuations for one lung as compared to the total of both lungs give an expression of the ventilation by that lung.

Time or phase relationships are displayed by simultaneous recording of respiration at the mouth and over the area by densiography. Ventilation is recorded by a spirometer or pneumotachygraph, although the latter is favored because of its low resistance and minimal inertia. Breath holding and rapid breathing permit identification of corresponding points on the recordings. The rapid breathing also shows alteration in phase and ventilation due to change of rate. A signal light blinking 60 times a minute establishes the rate.

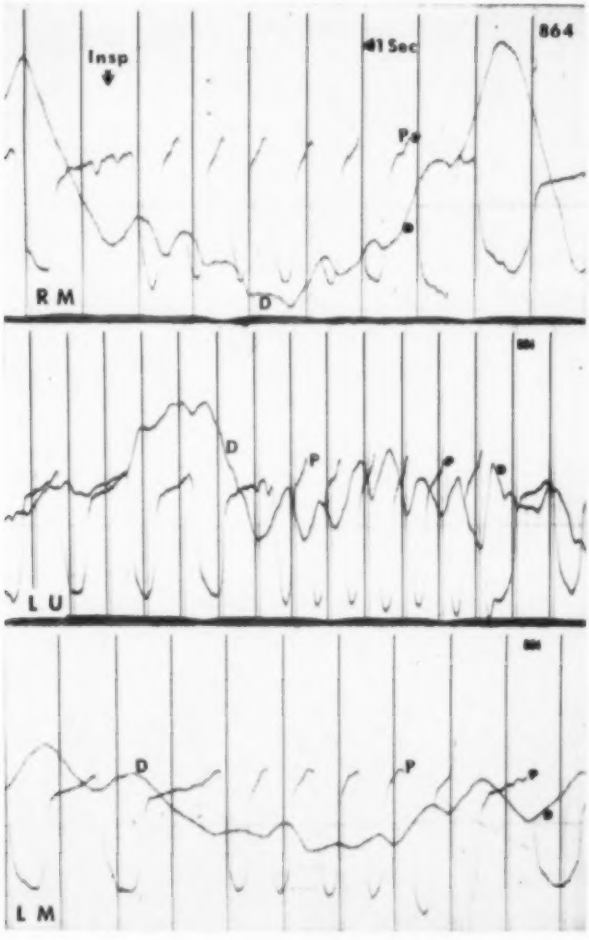

FIGURE 3: Male, 60 years. Diffuse obstructive pulmonary emphysema. Area: Right middle, left upper and left lower. Left upper shows reduced respiration and lags of 100° (corrected) but greater excursions at 60 respirations per minute than the right middle with normal phase and the left middle with a phase lag of minus 50° (corrected).

TABLE I
BRONCHOSPIROMETRIC AND DENSIOGRAPHIC EXAMINATIONS

No. 703 Female 61 years. Post-irradiational fibrosis of left lung (breast carcinoma).

	Ventilation			
	Right		Left	
		per cent		per cent
Bronchospirometry	5,375 cc./min.	75	1,750 cc./min.	25
Densiography		64		36

Results

During this study 50 patients and subjects were examined. This report is based upon the last 22 examinations, during which time no major modification was made in the technique.

Patients and subjects with normal lungs showed distribution of ventilation similar to those obtained by bronchospirometry. Two patients with unilateral radiation fibrosis showed marked reduction in ventilation on the involved side (Table I).

Patients with tumors showed increased density and decreased respiratory fluctuations. One patient, whose lung was removed the day following the examination, showed definite, though reduced, ventilation in spite of a severe chronic suppurative pneumonitis, bronchiolitis, bronchitis, and bronchiectasis.

One with bilateral pulmonary cysts and blebs showed progressive inflation in the area of a large cyst which suggested positive pressure in the cyst (Fig. 2). At thoracotomy (by Kenneth L. Morris) the cyst ballooned through the incision and was removed. The patient experienced great relief of dyspnea and returned to work after three weeks.

Respiratory fluctuations in diffuse obstructive pulmonary emphysema

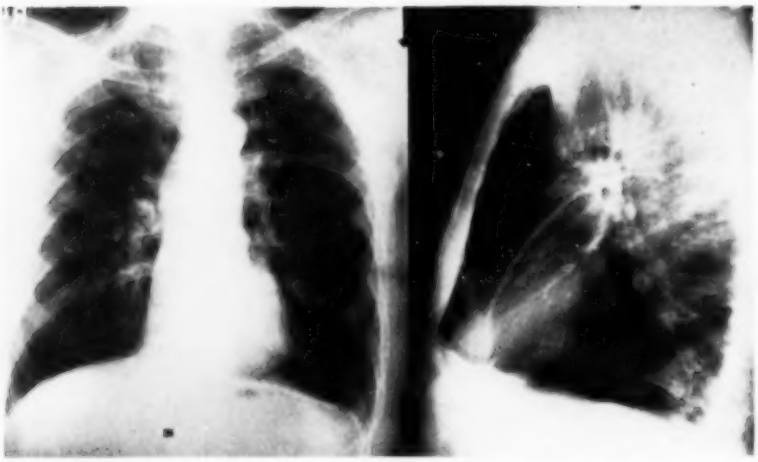

FIGURE 4: Diffuse obstructive pulmonary emphysema. Diagnosis of air sac replacement of left lower lobe was questioned (Table III).

were variable (Table II, Fig. 3) and no distinct pattern was identified. The chest x-ray film of one patient suggested a large air sac in the left lower lobe (Fig. 4). The densiogram showed good respiratory fluctuations in the left lower area with reduction in the left upper area so the diagnosis of an air sac was questioned (Table III). Thoracotomy revealed the left lobe to be extremely emphysematous with numerous blebs, but without sacs or bullae.

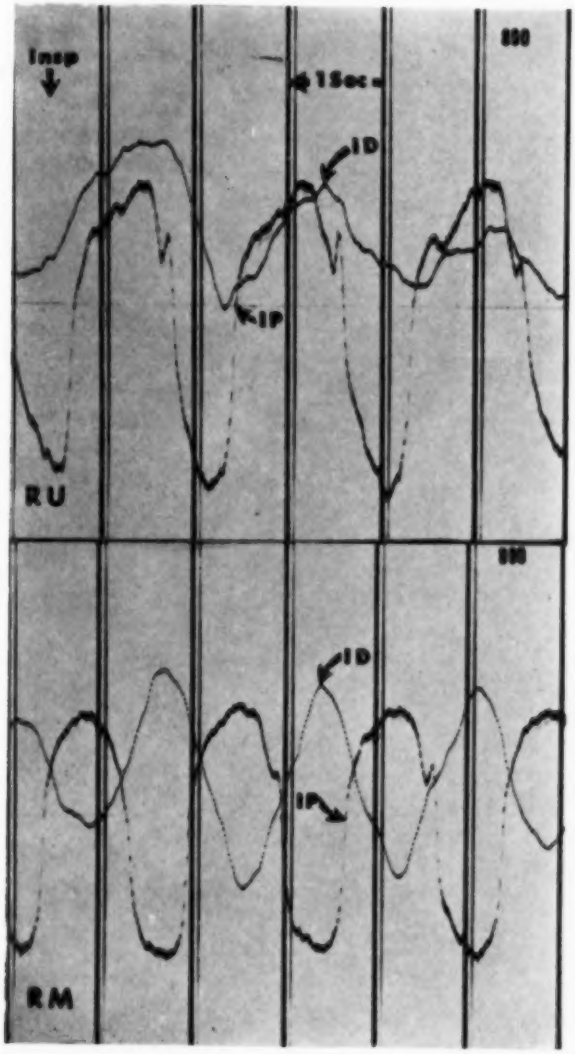

FIGURE 5: Fluoroscopic densiogram and pneumotachygram. Male, 58 years. Bronchogenic carcinoma of right upper lobe confirmed at pneumonectomy. Areas: right upper and middle lung "ID" and "IP" indicate the beginning of inspiration on the densiogram and pneumotachygram respectively. Over the shadow, breathing at the mouth lags breathing over the area by 180° observed or 260° corrected.

Below the shadow the densiogram lags 60° observed or 20° corrected behind the pneumotachygram. This is thought to be within normal limits.

TABLE II—FLUOROSCOPIC DENSIOGRAPHY REPORT

X-ray: 80 Kv., 1.5 Ma. Output 28 V. No. 864 April 3, 1958
Time: 7 min. 12 sec. 10.8 r. Photocell: 980 v. Amplifier: 7 ma. 150 v.

Area	Output, V.	Density, %	Respiration: Area V.	Respiration: Area %	Respiration: Lung, %	Respiration: Total, %	Respiration: Rate/min.	Respiration: Phase, °	Tachypnea: Rate	Tachypnea: Action
Right										
Upper	2.4	92	.205	12	39	23	25.6	0	73	Drift
Middle	2.4	92	.276	11	35	21	23.3	0	68	++ Drift
Lower	4.9	83	.400	8	26	16	24.6	0	92	Drift
Lung						60				
Left										
Upper	4.1	85	.157	4	19	8	28.7	100	65	+++
Middle	3.2	90	.327	10	48	19	24.0	−50	72	+
Lower	5.4	81	.297	7	33	13	27.9	200	50	++++
Lung						40				

TABLE III—FLUOROSCOPIC DENSIOGRAPHY

Area	Right per cent	Left per cent
Upper	23	14
Middle	29	40
Lower	48	46

Right lung 59 per cent. Left lung 41 per cent.

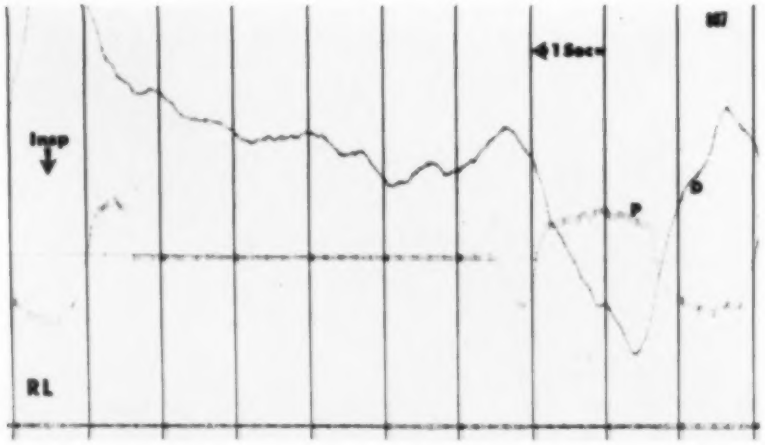

FIGURE 6: Fluoroscopic densiogram and pneumotachygram. Female, 50 years. Normal. Area: Right lower lung. Quiet breathing and breath holding. Quiet breathing is normal but during breath holding there is an expiratory drift followed by normal recovery. Insensible respiration may account for the drift.

Patients and subjects with normal lungs have minimal phase difference between the ventilation at the mouth and over the various areas.

One patient with an extra-pleural paraffin pack and three with localized bronchogenic carcinoma showed, over the shadow or adjacent to the shadow, that the respiratory fluctuations preceded the air movements at the mouth as demonstrated by the pneumotachygram (Fig. 5).

Patients with obstructive pulmonary emphysema demonstrated a definite lag in the ventilation of some areas behind the breathing at the mouth. No pattern was developed. In some patients this lag disappeared during voluntary tachypnea; in some, air flow continued at a slow rate during breath holding, however, this may be failure of complete cessation of respiration (Fig. 6). In one the phase lag disappeared after an intermittent positive pressure breathing treatment with a bronchodilator aerosol only to reappear in another area (Fig. 7).

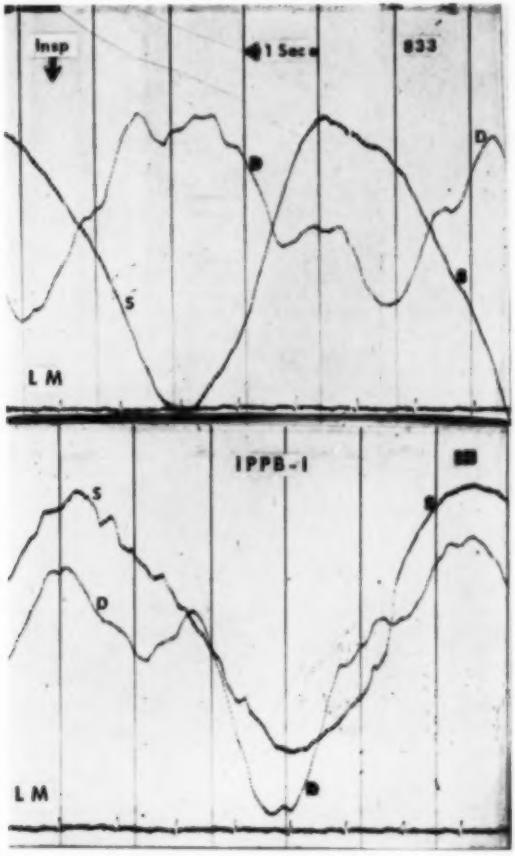

FIGURE 7: Fluoroscopic densiogram, spirogram and electrocardiogram. Male, 57 years. Obstructive pulmonary emphysema. Area: Left middle lung. Quiet breathing before and after intermittent positive pressure breathing, inspiration with 0.5 cc. Isoproterenol hydrochloride. A lag of approximately 180° before is normal after the therapy.

DISCUSSION

During inspiration the volume increase of the chest cavity produces stretching and thinning of pulmonary structures. This causes the fluoroscopic beam to traverse less tissue with less absorption and greater output, which is the commonly observed brightening of the lung fields. Fluoroscopic densiography is a method of recording this phenomena but with a degree of sensitivity greater than visual perception and confined to small areas. This method has been criticized on the basis that the anterior-posterior movement of the chest, being greater in the superior than in the inferior areas, would produce inaccuracies. If the lungs are perfectly elastic, the thinning of the structures will be of similar order regardless of the direction of maximum chest wall movements. In the absence of localized disease, expression of the total respiratory fluctuations of one lung as a percentage of the total of both lungs gives figures similar to those developed by bronchospirometry, that is, right 55 per cent and left 45 per cent. This suggests reliability of the data.

Fluoroscopic densiography is related only to ventilation and, unlike bronchospirometry, it gives no indication of lung function in terms of oxygen consumption. It possesses an advantage over bronchospirometry or bronchial catheterization by requiring neither local anesthesia, premedication nor the introduction of tubes which present a degree of obstruction to air flow and possible alteration of respiratory reflexes. The mental strain for the patient is minimal. Radiation exposure necessitates limitation of the duration and x-ray factors in this type of examination, although the exposures used are less than with most fluoroscopic examinations of the stomach. Low x-ray factors, minimal exposure during placement of the orifice, use of small shutter openings, automatic timing of exposure, radiation shielding, and calibration of the tube output are utilized to control exposure.

All measurements are made in the anterior-posterior axis. Overlapping of lobes except over the infraclavicular space, occurs so the terms "middle" and "lower" apply to areas and not to lobes. Recordings over the left lower lung areas are apt to be distorted due to mechanical compression by cardiac pulsations.

In addition to the lungs themselves, the x-ray density of the chest is affected by size, body build, muscular development and amount of adipose tissue, as well as by the distance of the orifice from the tube and patient, and to a lesser extent by the size of the shutter opening. No attempt has been made to attach significance to the absolute value of the density or the respiratory fluctuations. Breast density in the lower lung areas and well developed pectoral muscles reduce respiratory fluctuations.

Phase differences between air flow in different areas of the lung result in flow of air from one area into another, termed "pendelluft," and may contribute to the sequential ventilation of Fowler.[1] Such uneven ventilation produces inefficiency in ventilation and is strongly suggested by these observations. The phase differences observed were so extreme as to question their validity. Phase differences produced by the circuitry were recognized, measured and correction factors developed. Phase differences due to a rib or scapula moving into and out of the field were considered, but it was impossible to show that such artefacts produced the phase abnormalities. A columnating orifice was tried but rib movement made such violent fluctuations that it was abandoned.

It is difficult to explain the phase differences by the analogies, described by Olsen, between acoustical air flow systems composed of pressure, resistance and inerctance, and mechanical and electrical systems.[4] The change in phase between quiet breathing and voluntary tachypnea suggests that these factors are pertinent. To explain the phase alterations solely on the basis of lung compliance or obstruction is of doubtful accuracy. Obstruction to air flow in a subject, and compliance and air flow resistance differences in models, produce phase alteration, as shown by Otis, but not to the extent observed in this study.[2]

The lesions seen in the patients with reversal of lag were characterized by extreme stiffness or minimal compliance. These relatively unyielding masses may transmit pressure changes much more rapidly than the normal lung. This observation suggests that an additional factor exists, that is, the transmission of pressure through the lung parenchyma by continuity of lung architecture and its contents. This factor may act in addition to the factors effecting phase relationship of the air flow system and account for the extreme phase differences observed.

SUMMARY

A preliminary report is presented of fluoroscopic densiography as a method of pulmonary function study which approaches measurements of pulmonary ventilation over small areas of the lungs. After passage through the chest, the x-ray beam is transferred into electrical energy, modified and recorded on a strip chart.

Fluoroscopic density is expressed as a percentage of the x-ray absorption. Respiratory fluctuation in an area is expressed as a percentage of the transmitted x-ray by the chest in that area. The fluctuation may be expressed as a percentage of the total fluctuation of one lung. The total fluctuation of one lung may be expressed as a

percentage of the total of both lungs. These densities and fluctuations are altered in disease.

Time relations between air flow at the mouth and the respiratory fluctuations show phase relationships varying from normals of zero to lags as high as 140 degrees in obstructive pulmonary emphysema and the opposite of lesser degree in bronchogenic carcinoma.

This preliminary study suggests that fluoroscopic densiography may offer a valuable addition to pulmonary function studies in normal and disease states and may contribute diagnostic criteria.

RESUMEN

Se presenta una comunicación preliminar sobre la densografía como método de estudio de la función pulmonar que tiende a obtener medidas de la ventilación pulmonar sobre áreas pequeñas del pulmón. Después de pasar a través del tórax el haz de rayos X, se transforma en energía eléctrica que se modifica y se registra en una gráfica.

La densidad fluoroscópica se expresa como un porcentaje de la absorción de Rayos X. La fluctuación respiratoria en un área se expresa como porcentaje de los rayos X transmitidos por el tórax en esa área. La flucturacion puede expresarse como un porcentaje de la fluctuación total de un pulmón puede expresarse como un porcentaje del total de ambos pulmones. Estas densidades y fluctuaciones están alteradas en la enfermedad.

Las relaciones de tiempo entre la corriente de aire en la boca y las fluctuaciones, muestran relaciones de fase variando desde normales de cero hasta puntos tan altos como 140° grados de enfisema obstructivo y lo opuesto en menor grado en el carcinoma bronquiogénico.

Este estudio preliminar sugiere que la densografía puede ofrecer un agregado valioso a los estudios de la función pulmonar en los estados normal y patológico y puede contribuir a formar un criterio diagnóstico.

RESUME

L'auteur présente un rapport préliminaire sur la densigraphie radioscopique comme procédé d'étude de la fonction pulmonaire. Cette méthode permetude mesurer la ventilation pulmonaire sur de petites zones des poumons. Apres passage à travers le thorax, le rayon X est transformé en énergie électrique, modifié et enregistré sur bande.

La densité radioscopique est exprimée en pourcentage d'absorption radiologique. La modification respiratoire dans la zone est exprimée en pourcentage des rayons transmis par le thorax dans cette zone. La modification peut être exprimée comme le pourcentage de la modification totale du poumon. La modification totale d'un seul poumon peut être exprimée comme un pourcentage de la modification totale des deux poumons. Ces densités et modifications sont altérées dans les cas pathologiques.

Les rapports de temps entre le débit de l'air mesuré à la bouche et ces modifications respiratoires montrent des coefficients variant de la normale (zéro) à des retards atteignant 140 degrés dans l'emphysème pulmonaire obstructif et au contraire à un degré peu élevé dans le cancer bronchique.

L'étude préliminaire permet de penser que la densigraphie radioscopique peut offrir un procédé valable supplémentaire pour l'étude de la fonction pulmonaire dans les états normaux et pathologiques et peut contribuer à apporter des éléments de diagnostic.

ZUSAMMENFASSUNG

In Form einer vorläufigen Mitteilung wird berichtet über Leuchtschirmdensographie als einer Methode der Lungenfunktionsprüfung, die Messungen der Lungenventilation über schmalen Lungenabschnitten angeht. Nach seiner Passage durch den Brustkorb wird der Röntgenstrahl in elektrische Energie verwandelt, modifiziert und auf einem Karton-Reifen aufgezeichnet. Die Leuchtschirmdichte wird ausgedrückt als ein Prozentsatz der Röntgenstrahlenabsorbtion. Die respiratorische Schwankung eines Gebietes lässt sich ausdrücken als Prozentsatz der in dem betreffenden Abschnitt durch den Brustkorb geschickten Röntgenstrahlen. Die Schwankung kann als Prozentsatz der Gesamtschwankung einer Lunge ausgedrückt werden. Die Gesamt-Atemschwankung einer Lunge kann als ein Prozentsatz der totalen Atemschwankung beider Lungen ausgedrückt werden.

Diese Dichten und Schwankungen sind bei Krankheiten verändert. Zeitliche Relationsbilder sich als ein wertvoller Zuwachs erbietet für Lungenfunktionsprüfungen bei zeigen Zusammenhänge der Phase, die variieren von normalen Nullwerten bis zu Zeitabständen von Werten bis 140 Grad beim stenotischen Lungenemphysem und dem Gegenteil von geringeren Graden beim Bronchus-Carzinom.

Diese vorläufige Untersuchung lässt die Erwartung zu, dass die Leuchtschirmdensoggraphie sich als ein wertvoller Zuwachs erbietet für Lungenfunktionsprüfungen bei normalen und bei krankhaften Befunden und dass sie diagnostische Kriterien erbringen kann.

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A Resectable Form of Multiple Mesothelioma*

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Numerous reports in recent years have attempted to define the subject of mesothelioma of the pleura—its origin, pathology, natural course and treatment. The multiplicity of pathological descriptions well might lead one to ask if such a disease is a single entity or several different neoplasms.

The successful treatment of these tumors has been limited to the solitary form, some of which are benign. It has been generally conceded that successful treatment of the diffuse form, which is characterized by widespread pleural distribution, is not attainable. The object of this report is to indicate that surgically treatable forms of diffuse pleural mesothelioma exist but may remain untreated because of their deceptive appearance microscopically, particularly in the frozen sections. We are reporting on three cases of surgically treated mesothelioma of the pleura which had certain gross and microscopic characteristics in common. Of these three cases, one is living and well after five years,[1] and another more recent case is alive and well six months[2] after surgery.

E. S. This 43 year old white woman developed pain in the right chest two years prior to surgery. Pleural effusion was present. There was no history of cough, hemoptysis, chills, fever, or weight loss. Dyspnea was absent. X-ray films of the chest (Figure 1) after withdrawal of fluid and instillation of air showed multiple masses on both the parietal and visceral pleurae. The fluid showed mesothelial cells of no diagnostic importance.

On December 21, 1951 right thoracotomy was performed (by Dr. A. Goldman). The entire visceral and parietal pleurae were studded with opaque grayish nodules. A moderate quantity of bloody pleural fluid was present. One lymph node was taken from the subcarinal area; no other mediastinal node was seen. Frozen sections were reported as adenocarcinoma. The abdomen was entered and no involvement was noted

[1]At 6½ years, as of August, 1958, a small localized chestwall recurrence was treated.
[2]Two years, as of August, 1958.

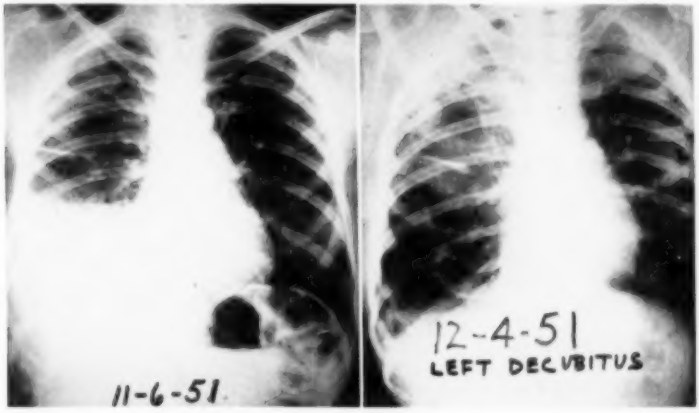

FIGURE 1

*From Cedars of Lebanon Hospital

of the liver. The surgeon elected to perform definitive surgery consisting of radical pleuro-pneumonectomy. The patient is living and well, five plus years after surgery (Figure 2).*

The frozen section diagnosis was metastatic adenocarcinoma, of the pleura. The surgical specimen consisted of the entire right lung enclosed within markedly thickened parietal and mediastinal pleural membranes and adherent diaphragm. Firm, pale tan tumor tissue all but obliterated the pleural surfaces as it formed innumerable discrete smooth nodules up to 3 cm. in diameter and cobblestone confluent sheets up to 2 cm. thick over the lung surface and in the interlobar fissures. Adhesions of the pleural surfaces were numerous. While the larger nodules compressed the lung from without meticulous dissection failed to reveal any true parenchymal lesions. Microscopically, the tumor was composed of irregular cords and sheets of large polygonal cells with abundant cytoplasm and uniform large oval vesicular nuclei in which one or two dot-like nucleoli were prominent. Scattered areas revealed the space lining proclivity of the tumor as the plump cells formed linings around irregular slits and anastomosing crypts and pseudoglands. The stromal component varied from a loose collagen reticulum mesh to dense fibrotic sheets. Mitotic figures were quite rare but slight hyperchromatism and nuclear atypism was noted in peripheral areas. The hilar lymph nodes were not involved but superficial invasion of the diaphragm was present. The final diagnosis was mesothelioma (Figures 3, 4 and 5).

S. S. This 51 year old white man was in good health until a "few months" prior to admission when he developed general malaise. He had an acute upper respiratory infection followed by right chest pain and dyspnea of several weeks duration. X-ray film showed a pleural effusion. Thoracentesis yielded fluid in which tumor cells were found. Air injection revealed multiple pleural tumors.

On December 7, 1954 thoracotomy was performed with the finding of involvement of the entire pleural surface, both visceral and parietal. There was no liver involvement. The frozen section was reported as "papillary adeno-carcinoma of the pleura,

*See footnote 1 on first page.

FIGURE 2

possibly metastatic, possible mesothelioma." Because of this report, the situation was deemed hopeless and the chest closed. He was reoperated on June 21, 1955, but complete removal of all visible tumor was no longer possible. The pathological diagnosis on the permanent paraffin sections was "mesothelioma of the pleura." He expired December 31, 1955 with widespread involvement of the chest wall, mediastinum and pericardium.

The original biopsy on December 7, 1954 consisted of a strip of thickened pleura studded with small firm tan tumor nodules. The frozen section diagnosis was adenocarcinoma although one of the staff pathologists who examined the material at the time of surgery favored a diagnosis of mesothelioma. Microscopically, the nodules showed short broad papilli projecting into irregular clefts and connecting spaces and lined by quite uniform plump polygonal cells. The papillary pattern predominated, but in some areas sheets of cells were seen and, rarely, discrete anastomosing crypts without papilli noted. The final diagnosis was metastatic papillary adenocarcinoma or mesothelioma. The second specimen on June 21, 1955 was a resected lung, encased in its upper portion by confluent nodules of smooth glistening tumor and studded in all areas by plaques and nodules of similar tissue. The tumor extended into the interlobar fissures but was grossly confined to the surface. No parenchymal lesion could be found. Microscopically, the tumor cells remained remarkably uniform, although some nucleoli now appeared atypical and unusually prominent. In several sections the space lining tendency overshadowed the papillary differentiation of the earlier biopsy. The hilar nodes were not involved but tumor infiltrated the lung superficially and penetrated into the retropleural fat. The final diagnosis was mesothelioma.

At autopsy on December 31, 1955 the tumor, while quite widespread, was chiefly limited to the serosal surfaces. The smooth nodular plaques studded pleura, pericardium and particularly peritoneum. A few superficial nodules within the liver were the only parenchymal lesions discovered. Microscopically, the tumor had assumed a much more pleomorphic and aggressive pattern. Crypts and papilli were replaced by large sheets of cells retaining only superficial resemblance to the primary biopsy. Dense fibrous nodules containing but few compressed cells were numerous, while in the liver clear cut transition of pleomorphic polygonal cells to loose spindle cells and thence to fibrotic hypocellular masses was apparent.

Papanicolaou smears on the ascitic fluid during life were read as Class IV (suspicious of malignancy). This is of interest since fluids from mesotheliomas are often under-read because of the similarity of the neoplastic elements to the normal and hyperplastic mesothelial cells seen in non-neoplastic effusions (Figures 6 and 7).

FIGURE 3

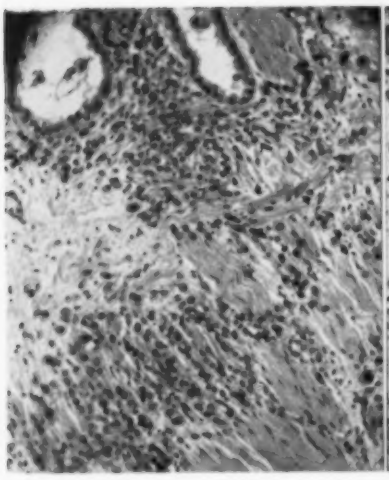

FIGURE 4

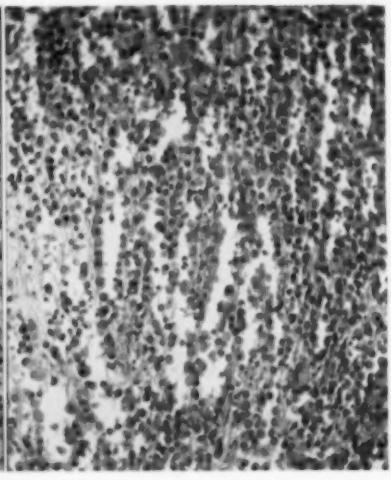

FIGURE 5

B. P. This 37 year old white woman developed pain in the anterior portion of the right chest three years prior to surgery. Two months prior to her admission an x-ray film taken by a mobile unit showed a lesion in the right chest. She denied hemoptysis, chills, fever, weight loss or cough. X-ray film showed multiple large masses over the right middle and lower lobe areas. Thoracentesis did not yield fluid and the pleural space apparently was obliterated (Figure 8).

With a preoperative diagnosis of mesothelioma of the pleura right thoracotomy was performed on August 9, 1956. All the pleural surfaces of the right hemithorax were involved in masses of tumor tissue. The frozen section was reported as adenocarcinoma. A radical pleuro-pneumonectomy was performed. The patient is doing well six months* after surgery.

The frozen section diagnosis was adenocarcinoma. The surgical specimen consisted

*Now two years.

FIGURE 6

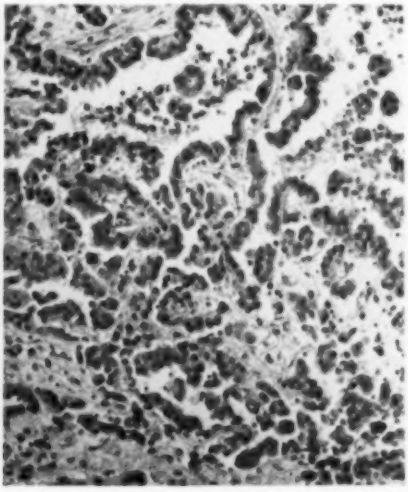

FIGURE 7

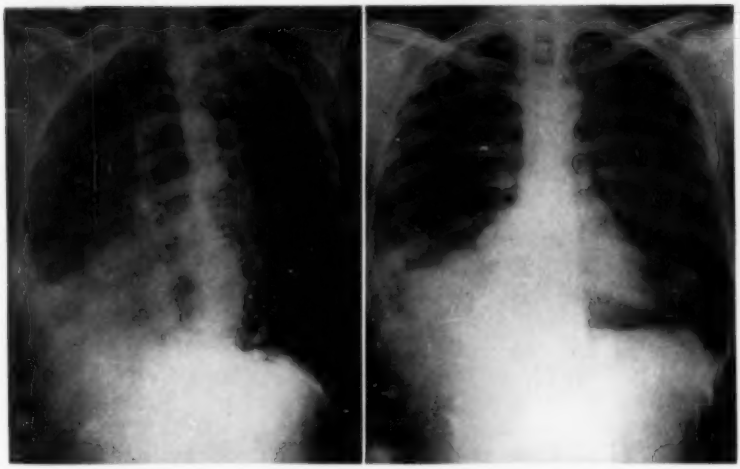

FIGURE 8

of a 925 gram right lung, the lower and middle lobes of which were covered by nodular masses and plaques of firm tan tumor. The plaques varied in thickness from 1 to 4 cm. while the larger nodules, up to 5 cm. in diameter, compressed but did not invade the subjacent lung. Careful dissection revealed no parenchymal or bronchial lesion. Microscopically, the tumor was composed of innumerable short fat papilli projecting into irregular anastomosing cleft and crypts. The lining cells were plump uniform polygonal cells, rich in cytoplasm and possessing regular vesicular nuclei with one or two dot-like nucleoli. Pavement-like sheets of these cells were present in the cleft spaces. The relatively abundant stroma formed a loose mesh in cellular areas, became dense and fibrous in peripheral areas, and assumed a peculiar hyalin appearance in most of the papillary cores. Mitotic figures were not seen or was invasion of the lung noted. There were pseudosarcoid granulomas in both lung and lymph nodes. The final diagnosis was mesothelioma (Figures 9 and 10).

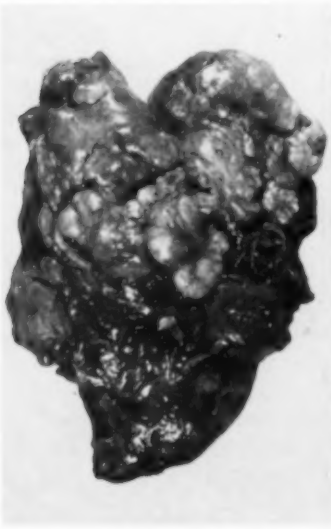

FIGURE 9

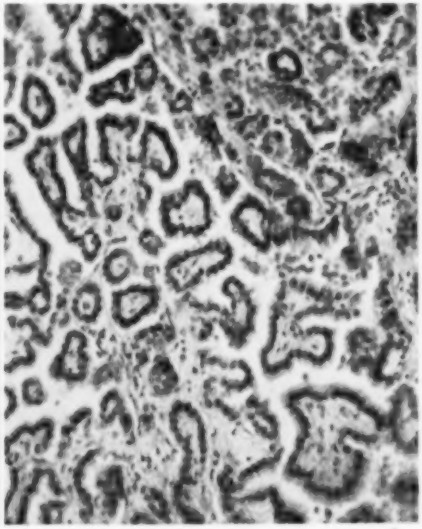

FIGURE 10

Discussion

At surgery it was noted that although the tumor masses over the parietal surface were quite hard and appeared to involve the underlying soft tissues, bone itself and deep structures were not invaded and the tumors were moveable. The diffusely spread masses could be stripped from the chest wall along with the pleura without resorting to rib resection.

Although at surgery the frozen section report of adeno-carcinoma would indicate anything but a successful result, it was decided on the basis of clinical judgment to proceed with radical resection. In fact, in the last case, guided by the experience of the previous ones, decision for radical surgery was made preoperatively in anticipation of a pathological report of adeno-carcinoma. The second case, on the basis of the frozen section was closed and later reoperated on, possibly resulting in a lost surgical opportunity.

The permanent paraffin sections of these three cases still bore a striking resemblance to adeno-carcinoma, but close study of these sections led to a differentiation not possible on the frozen tissue study. In all cases, the later studies were interpreted as mesothelioma of the pleura, pointing up the basic thesis of this report—the unreliability of the frozen section in diagnosing this tumor, and the need of clinical awareness of its deceptive appearance both microscopically and grossly. The alternative is reoperation at a later date when the permanent sections have disclosed the true nature of the lesion. In passing, it probably should be pointed out that if the question of mesothelioma is never raised in relation to these tumors, a hurried or less than careful examination of the permanent section might fail to reveal the correct diagnosis.

SUMMARY

Three cases of mesothelioma of the pleura are presented which were treated by radical surgery with one five year survival to date. The point is raised that the resemblance to adeno-carcinoma in frozen sections might lead the surgeon to abandon the operation in the belief that a hopeless situation exists. It is suggested that the pattern of clinical course, x-ray film findings and gross findings at surgery should raise the question of a resectable mesothelioma of the pleura in spite of a contrary pathological report based on a frozen section.

RESUMEN

Se presentan tres casos de mesotelioma de la pleura que se trataron con cirugía radical y sobreviven hasta ahora, después de cinco años. Se presenta la cuestión de que la semejanza con el adenocarcinoma en los cortes congelados puede llevar al cirujano a abandonar la operación en la creencia de que se trate de un caso fuera de todo recurso.

Se sugiere que el cuadro clínico, los hallazgos radiológicos y los obtenidos durante la operación, deben hacer plantear la posibilidad de un mesotelioma resecable a pesar del informe contrario a partir de un corte congelado.

RESUME

L'auteur présente trois cas de mésothéliome de la plèvre, qui furent traités par chirurgie radicale, avec survie de cinq ans. L'auteur soulève

le problème de la ressemblance avec l'adéno-carcinoma dans les coupes extemporanées qui pourrait amener le chirurgien à abandonner l'opération en croyant que la situation est sans espoir. L'auteur estime que le tableau de l'évolution clinique, les constatations radiologiques et les constatations d'ensemble pendant l'opération devraient faire soulever le problème d'un mésothéliome de la plèvre opérable, même quand le rapport anatomo-pathologique basé sur une coupe semble défavorable.

ZUSAMMENFASSUNG

Es werden 3 Fälle von Mesothelioma der Pleura vorgestellt, die mit einer radikalen Operation behandelt wurden und bis jetzt 5 Jahre überlebt haben. Es wird dabei darauf aufmerksam gemacht, dass die Ähnlichkeit mit dem Adenocarcinom auf Gefrierschnitten den Chirurgen veranlassen könnte, die Operation abzubrechen, im Glauben, dass eine hoffnungslose Situation vorliege. Es wird der Annahme Ausdruck gegeben, dass die Eigenheit des klinischen Verlaufes, der Röntgenbefund und der Makroskopische Befund während der Operation die Frage eines resektionsfähigen Pleura-Mesotelioms erwecken muss, trotz eines gegenteiligen pathologischen Befundberichtes auf Grund eines Gefrierschnittes.

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Clinical Experience with Ataractic Therapy in Tuberculous Psychiatric Patients

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When we learned of the efficacy of Rauwolfia serpentina products in managing psychoneurotic tension states and frank psychoses, we decided to try them on patients with both psychosis and tuberculosis. Practically, we hoped that the drugs would make the patients more cooperative in their treatment for tuberculosis. Theoretically, we thought that assuaging emotional turmoil might be a genetic attack against each of the two diseases we were trying to combat.

Our approach was based on the long-standing assumption that psychogenic factors influence the development and progression of pulmonary tuberculosis. In some patients the disease may cause an outright depression, but in most it probably sets up a state of anxiety and tension. For the psychotic patient with tuberculosis, control of his agitated, manic, or schizophrenic state is even more imperative if successful antituberculosis therapy is really to be accomplished.

In view of the often dramatic results reported from the use of the tranquilizing drugs, a study was set up to determine their possible value in a group of psychotic tuberculous patients. It was hoped that three things might be learned: (1) From a purely practical standpoint whether the drug makes the patients more cooperative toward accepting the treatment for tuberculosis. (2) Whether the tranquilizing drug would lessen the emotional turmoil. (3) Finally, what tranquilizing drug or what combination would be most efficacious. Although electroconvulsive therapy still has its place in the treatment of psychotic patients, there is frequently considerably hesitation about using it on active tuberculous psychotic patients, because of fear that convulsions may possibly activate or spread the disease. It was, therefore, thought that a less violent method of controlling disturbed behavior would be very advantageous.

Methods and Materials

Over the past two years, 235 patients were chosen for treatment with various tranquilizing drugs. All patients had active pulmonary tuberculosis and suffered from a major psychosis. The psychosis fell into one of the following categories: Chronic manic psychosis, depressive psychosis, chronic brain syndrome, or one of the various types of schizophrenia, the duration of the psychoses being anywhere from one to nine years. The patients' behavior ranged from hyperactive, noisy, and combative to regressed and seclusive states. All of the treated patients were aggressive, destructive and unpredictable, and some were in restraint. Most of them refused oral antimicrobial therapy, and were uncooperative and difficult to manage.

Standard antituberculosis medications were used including streptomy-

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cin, isoniazid, para-aminosalicylic acid, and in occasional instances viomycin. Regardless of which "tranquilizing" drug or drugs were used, the dosage for each patient was adjusted according to his individual response.

Seventy patients were treated with an alkaloidal extract of Rauwolfia serpentina, namely, Alseroxylon* for a period of seven months.

Initially, fairly large dosages of Alseroxylon were necessary for an adequate response. Some patients required daily dosages of as much as 48 mgm., divided into four doses. With the onset of tranquilization, the dosage was individually reduced until a satisfactory maintenance level was established. The average acceptable maintenance dosage was about 24 mgm. of Alseroxylon daily, in divided doses, although a smaller amount of the drug was satisfactory in some instances.

In certain considerably excited or acutely disturbed patients, some of whom were in need of temporary restraint, parenteral therapy was required in the initial stages. Reserpine** was administered intramuscularly, in dosages of 5 mgm. daily in these cases. In all cases, Alseroxylon was given orally, either concomitantly with parenteral therapy or on alternate days. Patients varied in their responses, but we could usually carry them on Alseroxylon as the only "sedative" within a week or ten days from onset of therapy.

The second group consisting of 68 patients, 21 of whom had been started on Rauwiloid, were treated with Serpasil.* Most of the patients in this group received the drug initially by parenteral route and were later switched to oral medication. The dose ranged from 0.5 mg. to 5 mg. per day. The results are based on 14 months of treatment.

The third group of 120 patients, 37 of whom had first been on Alseroxylon, were treated with chlorpromazine** for 14 months. For these patients the dosage ranged from 150 mg. to 900 mg. per day.

The fourth group is still being treated with a combined dosage of Serpasil and chlorpromazine. Generally 1 to 3 mg. of Serpasil and 75 to 150 mg. of Thorazine are given daily. This latter group has only been on this combination therapy for seven months.

Results

There was a definite, general, over-all improvement in both the psychiatric and tuberculous status of the patients. In all groups there was a tendency to gain weight. Better social adjustment was seen in the patients' attitude toward accepting ward duties, helping one another, and responding to group psychotherapy.

Improvement was most noticeable in acutely disturbed patients who formerly were given to frequent belligerent and combative outbursts. To some degree, all patients appeared to benefit from therapy; their symptoms of anxiety, tension, confusion and psychomotor excitement were reduced. Instead of a jail-like atmosphere, with nurses and attendants as the constabulary, the wards became hospital-like in the true sense. Combative outbursts, destruction, and restraints became things of the past.

*Rauwiloid, Riker Laboratories, Inc., Los Angeles, California.
**Serpiloid, Riker Laboratories, Inc., Los Angeles, California.
*Ciba.
**Thorazine SKF.

TABLE I
TUBERCULOSIS AND PSYCHIATRIC STATUS

Drug	No. Pts.	Tuberculosis Status		Psychiatrically Discharged	
		Improved	Inactive	Number	Per Cent
Serpasil	68	27	32	27	40
Rauwiloid	70	32	28	12	17.1
Thorazine	120	43	69	41	34.2
Combined*	35	24	7	14	40

*Combined Serpasil and Chlorpromazine.

Without exception, all of the patients in our studies became quieter, more cooperative and began taking their antituberculosis medication much more readily. None of these patients required further restraints.

In summarizing there was tremendous improvement in the patients' psychiatric condition in about 85 percent of the cases. See Table I.

The percentage of psychiatric improvement was sufficient to permit psychiatric discharge of 40 per cent for those on Serpasil, 34.1 per cent for those on Thorazine, and 40 per cent for those on combination therapy. The response was fastest when combined Serpasil and Thorazine was used, next with Thorazine alone, and then with Serpasil alone. The response to all drugs was poorest in those patients with an endogenous depression.

Rauwolfia should not be used in psychoneurotic patients with depressive states as it may aggravate their depression.

Another important, though indirect, effect of our therapy deserves mentioning—the effect of the tranquilizing drugs on the course of the tuberculous condition. A comparison of roentgenograms during and after therapy revealed improvement in many cases, no doubt because the patients were quiet and better rested, and more receptive towards the usual chemotherapeutic treatment.

Although no such action has been reported at the Ciba Laboratories in Summit, N. J., upon our request a study was set up to determine whether Serpasil might have an antituberculosis action.

At the Ciba Laboratories, the mice infected with human strain (H37Rv) tuberculosis, varying doses of Serpasil given both orally and intraperitoneally did not show any bacteriostatic or bactericidal effect.

Side Effects

In our studies of the four groups of patients, no serious adverse effects which could be attributed to the ataractic medication were noted. The side effects encountered were the same as those which had been reported by many investigators. See Table II.

Discussion

Tranquilizing drugs are of great benefit in both the antituberculosis and the psychiatric management of patients. As high as a 40 per cent psychiatric discharge rate was achieved with ataractic medications. The combined therapy, namely, Serpasil and Chlopromazine seems to accomplish this more rapidly.

TABLE II
SIDE EFFECTS

Serpasil	Thorazine	Rauwiloid	Combination*
Unsteady gait	Skin eruption	Nasal stuffiness	Jaundice
Tremor (Parkinson-like symptoms)	Jaundice (1 case)	Drowsiness	Dermatitis
Lassitude & Depression	Parkinson Syndrome		Orthostatic hypotension
Diarrhea & GI hemorrhage (1 case)	Constipation		Drowsiness
Dizziness (Orthostatic hypotension)	Dizziness (Postural hypotension)		Occasional complaints of gastritis

*Thorazine and Serpasil combined.

Endogenous depressions are not helped to any degree by these compounds. As Ayd has said, although these drugs probably do not cause depression, they can unmask latent depression.

The tuberculous process improved in approximately 90 per cent of the patients. The tuberculous condition of a great number of them in our groups were static before the tranquilizers were employed. It would seem that the results achieved are sufficient proof for our assumption that tranquilizing drugs have a beneficial effect on the emotional status as well as the somatic condition in N P-tuberculous patients. The improved nutritional status effected by the ability of ataractic drugs to increase the appetite is unquestionably a help to the patient with tuberculosis. Furthermore, these patients were more amenable to specific tuberculosis therapy and were better able to accept institutional care. As to the drugs and dosage routine, the best results have been achieved by a combination of Serpasil and Thorazine. The dosage, however, must be individualized.

SUMMARY

(1) Various combinations of tranquilizing drugs were given to four groups of neuropsychiatric tuberculous patients. Rauwiloid, Serpasil, Thorazine and a combination of the latter two drugs was used.

(2) Ataractics appear to be of value as an adjunct in the management and treatment of NP tuberculous patients. The majority improved sufficiently to permit psychiatric discharge and there was a definite beneficial effect of the tranquilizing drugs upon the course of the tuberculous condition.

(3) After comparing the actions of the various ataractic drugs, we found that the combination of Chlorpromazine and Rauwolfia Serpentina accomplishes the beneficial effect more rapidly.

(4) Ataractic drugs should be considered as an adjunctive therapy in NP tuberculous patients. The drug must be given in sufficient dosage and for a sufficient length of time in order to be therapeutically effective. Individualization of dosage is necessary.

(5) Serious side reactions were not encountered.

(6) It should be stressed that the ataractics used in our project failed to show antituberculous therapeutic properties per se.

Acknowledgments: We are indebted to Doctor Otto L. Bettag, Director, Department of Public Welfare, State of Illinois, and Doctor Kalman Gyarfas, Superintendent, Chicago State Hospital, for their advice and support in this project, and to Mrs. Ruth Fulcher, R.N., Supervising Nurse, Chicago State Hospital, and the members of her staff, for their continuous help in assisting with the treatment program and their invaluable detailed observations and reports.

RESUMEN

1. Se dieron varias combinaciones de drogas tranquilizantes a cuatro grupos de tuberculosos neuropsiquiátricos. Rauwiloid, Serpasil, Thorazine y una combinación de las dos últimas se usaron.

2. Parece que las drogas ataráxicas tienen valor como adyuvantes en el tratamiento de los tuberculosos neuropsiquiátricos. La mayoría mejoró bastante para ser descartados del grupo psiquiátrico y hubo un efecto favorable definido de las drogas tranquilizantes sobre la evolución de la enfermedad tuberculosa.

3. Después de comparar el efecto de las diversas drogas ataráxicas encontramos que la combinación de cloropromazina con Rauwolfia Serpentina logran efecto más rápido.

4. Las drogas ataráxicas deben considerarse como adyuvantes en la asociación de esas dos condiciones patológicas. Deben darse en dosis suficiente y por un tiempo suficientemente largo para que logre efecto. Es necesaria la dosificación individual.

5. No hubo reacciones colaterales serias.

6. Debe recalcarse que los ataráxicos usados en neustra experiencia no mostraron por sí ningún efecto antituberculoso.

RESUME

1. Différentes associations de drogues calmantes furent administrées à 4 groupes des malades neuropsychiatriques atteints de tuberculose. Nous avons utilisé le "Rauwiloïde," le "Serpasil," la "Thorazine" at une association de ces dernières médications.

2. Les calmants semblent être de grande valeur comme complément du traitement des malades neuro-psychiâtriques atteints de tuberculose. La majorité des malades furent suffisamment améliorés pour permettre leur sortie de l'hôpital psychiâtrique et nous avons observé un certain effet favorable des drogues "tranquillisantes" sur l'évolution de l'état tuberculeux.

3. Après avoir comparé les actions des différentes drogues calmantes, nous avons trouve que l'association de la chlorpromazine et du *rauwolfia serpentina* est celle qui produit le plus rapidement un effet favorable.

4. Les calmants devraient être considérés comme une thérapeutique complémentaire des malades de neuro-psychiâtrie atteints de tuberculose. La médication doit être donnée à dose suffisante et pendant une période suffisamment prolongée pour permettre l'effet thérapeutique. Il est nécessaire d'adapter la posologie à chaque individu.

5. On ne constata pas d'effets secondaires graves.

6. Il faut mettre l'accent sur le fait les calmants utilisés dans notre étude ne montrèrent pas de propriétés thérapeutiques antituberculeuses en eux-mêmes.

ZUSAMMENFASSUNG

1. Verschiedene Kombinationen von entspannenden Medikamenten wurden in 4 Gruppen von neuro-psychiatrischen Patienten mit Tuberkulose gegeben. Rauwiloid, Serpasil, Thorazin und eine Kombination der beiden letztgenannten Mittel wurde verwandt.

2. Ataraktika scheinen wertvoll zu sein als ein Hilfsmittel bei der Betreuung und Behandlung von neuropsychiatrischen Patienten mit Tuberkulose. Die meisten wurden so ausreichend gebessert, dass eine Entlassung aus psychiatrischer Behandlung möglich war, und es liess sich eine definitive günstige Wirkung auf den Ablauf des tuberkulösen Krankheitsgeschehens nachweisen.

3. Wir fanden nach einem Vergleich der Wirkungen der verschiedenen ataraktischen Mittel, dass die Kombination von Chlorpromiazin und Rauwolfia, Serpentina schneller zu einer günstigen Wirkeng führt.

4. Ataraktische Mittel können als zusätzliche Therapie für neuropsychiatrische tuberkulöse Patienten angesehen werden. Das Medikament muss in ausreichender Dosierung gegeben werden und für genügend lange Zeit, um therapeutisch wirksam sein zu können. Anpassung der Dosierung an den Einzelfall ist notwendig.

5. Ernsthafte Nebenwirkungen wurden nicht bemerkt.

6. Es muss hervorgehoben werden, dass die in unserer Untersuchung verwandten Ataraktika keine antituberkulösen Eigenschaften als solche zeigten.

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The Topographic Distribution of Mineral Dusts in Some Pneumoconiotic Lungs*

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All theories that have served to explain the formation of fibrous tissue in silicosis relate the development of the collagen fibers, directly or by inference, to the site of the silica particles. Recent studies[1, 2] have established that portions of some silicotic nodules may contain no demonstrable mineral particles and that dust particles formerly believed to be more or less permanently imprisoned at the site of their deposition within the lung tissue not only may be shifted from one region to another within the lung but may also be expectorated. Thus the occurrence of silicotic fibrous tissue without the demonstrable associated causative mineral particles should be considered no more anomalous than the more familiar finding of manifestly silicotic lungs with a relatively low silica content, that is, a silica content no higher than that of some non-silicotic lungs.

Because the topographic study of the distribution of mineral dust in pneumoconiotic lung tissue gives promise of providing new information regarding the pathogenesis of pulmonary dust diseases such studies have been performed on routine cases that have come to the attention of the Industrial Hygiene Foundation. It is the purpose of this paper to summarize the results of some of these studies.

Method

Formalin-fixed lung tissue was embedded in paraffin, sectioned and stained in a routine manner. In addition replicate sections were also stained by a combination of the Van Gieson stain for collagen and the postassium ferrocyanate method for iron. The locations of selected fields in the stained sections were noted with the aid of a "field finder."† Following photography of these fields, the sections were incinerated at 550° for one hour, and after cooling, the acid-soluble portion of the ash was removed by placing the slides in concentrated hydrochloric acid for 30 minutes. They were then washed with running tap water, followed by rinsing in distilled water and air drying. The same fields were then rephotographed but under dark field conditions. Composites were made by superimposing the 2¼" x 2¼" dark-field negative upon the bright-field negative or the color transparency of the same field and after careful matching, fixing them in their relative position by means of transparent tape.

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*Presented at the 23rd Annual Meeting, American College of Chest Physicians, New York City, May 29-June 2, 1957.

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†Sold by W. & L. E. Gurley, Engineering Instruments, Troy, N. Y.

Observations

1. *Silicosis with slight asbestosis*

Case O. S. G., age 55, had 31 years exposure to fine silica sand (consistency of flour) and to a minor degree also to cement and asbestos dust. Patient had worked steadily until 17 months prior to death. X-ray at the onset of illness showed a spontaneous pneumothorax and generalized pulmonary nodulations (Figure 1). He continued to work, but intermittently, until two months prior to death. The main pulmonary findings at autopsy included severe silicosis with minimal asbestosis, emphysema, and sclerosis of pulmonary vessels.

Analysis of the dried lung indicated a total silica content of 1.77 per cent (chemical determination) and a quartz content of 1.0 per cent (x-ray diffraction).

Most of the lung sections show relatively little air-containing tissue. Much of the tissue is represented by silicotic nodules and masses which, although composed of acellular hyaline, show no lamination. Many of the nodules, particularly the smaller ones, have a stellate or irregular periphery (Figure 2). The nodules contain a surprisingly small amount of mineral dust much of which is concentrated on the periphery (Figure 4). The larger nodules and masses generally contain less dust than the smaller ones. There are regions (Figure 6) such as where air spaces are all but surrounded by coalescent nodules in which the walls of air spaces are diffusely infiltrated by dust. Asbestos bodies are seen in this region associated with foci giving a positive reaction for iron.

2. *Pure Silicosis*

Case J. C., age 72, had been a monument worker for 27 years to the age of 47. For the next ten years he was a door-to-door salesman and the following ten years were spent as a supervisor of several small apartment buildings. At the time of his death, in addition to silicosis there was a renal carcinoma with small pulmonary metastases and a penetrating duodenal ulcer with subdiaphragmatic abscesses.

Sections of lung contain sharply delimited, laminated and well collagenized nodules which vary in size from microscopic to 4 mm. in diameter and larger (Figure 7). The intervening lung tissue is emphysematous and the pleura is thickened. The nodules are composed of acellular, concentrically arranged hyaline collagen which is surrounded by a cellular "reactive" zone of varying width (Figure 8). Although the

FIGURE 1: Case O. S. G. Advanced pneumoconiosis due to mixed dusts: quartz silica, cement, and asbestos.

collagenous portions of most nodules are smooth and rounded, and even the peripheral reactive zone frequently also presents a smooth and rounded circumference, there are regions which resemble a sunburst (Figure 10). This appearance is produced by a fibrous thickening of the bases of adjoining septa that extend radially. The collagenous centers of the nodules contain irregularly scattered aggregations of mineral dust with considerable portions of the collagen free of demonstrable dust. In contrast, much of the mineral dust is concentrated in the peripheral reactive zone, extending also into adjoining septa (Figures 9 and 11).

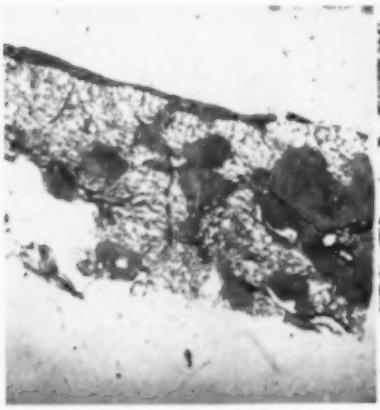

FIGURE 2

FIGURE 3

Figure 2: (Neg. 3360) Case O. S. G. Single and coalescent, nonlaminated silicotic nodules with partially smooth, and partially stellate contours. Emphysema and fibrous pleural thickening. Van Gieson-iron stain.—*Figure 3:* (Neg. 3303) Case O. S. G. Two coalescent fibrous nodules, the lower one possessing a "reactive" peripheral zone. Van Gieson-iron stain.

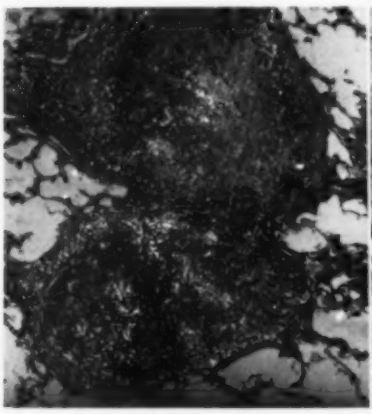

FIGURE 4

FIGURE 5

Figure 4: (Neg. 3303) Case O. S. G. Composite of the above showing relatively little mineral dust in center of nodules, less in the larger one than in the smaller. Concentration of mineral aggregates in the peripheral "reactive" zone.—*Figure 5:* (Neg. 3304) Case O. S. G. A cluster of coalescent nodules surrounding a small island of atelectatic alveoli. The darkly staining spots are largely siderophages and asbestos bodies situated in the atelectatic tissue. The nodules are largely hyaline but show a peripheral, cellular, "reactive" zone. Van Gieson-iron stain.

3. *Silicotuberculosis with slight asbestosis*

Case S. G., died at age 48, nearly 11 years after his last exposure mainly to silica (as diatomaceous earth) and to a lesser degree to asbestos. The total duration of dust exposure was nine and one-half years. He was forced to quit his job and to be institutionalized for six years because of tuberculosis. Following his discharge he performed light work for almost three years but was forced to seek readmission because of serious illness with positive sputum. The patient died 21 months after his last admission.

The results of a post-mortem examination indicated that death was due to an extensive tuberculous pneumonia which arose from a cavitating fibro-caseous tuberculosis of the lungs. There was a severe pneumoconiosis in which silica (as cristobalite) played a major role and asbestos, a relatively minor role. Right ventricular hypertrophy and dilatation (cor pulmonale) were present.

The silicotic nodules here are non-laminated and, as in the preceding cases, contain a moderate amount of mineral dust which tends to be concentrated at the periphery. The smaller nodules are stellate because of broad fibrous thickening of the bases of radiating alveolar septa (Figure 13). The mineral dust tends to extend beyond the nodules into the adjoining, widened alveolar septa (Figure 14). The larger nodules and masses, on the other hand, contain much less mineral dust. The outlines here are not stellate because adjoining septa are not thickened and no mineral dust is demonstrable beyond the confines of the nodules or masses.

Circumscribed areas of caseous necrosis are singularly devoid of mineral dust (Figure 16). There is likewise a striking paucity of mineral dust in areas of other tuberculous inflammation except in a region of tuberculous pneumonia where mineral dust is found in a few of the thickened alveolar septa which are still viable, and in the adjoining caseous alveolar content.

Some regions rich in asbestos bodies also contain many coarse and fine asbestos fibers of varying lengths, but no relationship can be demonstrated between the asbestos bodies and the asbestos fibers.

4. *Diatomite Pneumoconiosis*

Case E. S., died at age 71. Beginning with age 42 and continuing for 12 years to age 54 there was exposure to natural, calcined, and fluxcalcined diatomite powders in varying concentrations. Following recovery from an acute attack of coronary heart disease at age 54 he was transferred to office work with no more occupational exposure. A second attack three years later forced his retirement at age 57. For the next 14 years until his death the patient led a sedentary life, doing no work. During this last period there was a gradual increase in respiratory impairment. He died of cardiac and respiratory failure following an attack of bronchopneumonia.

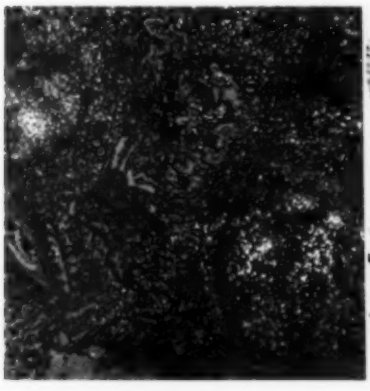

FIGURE 6

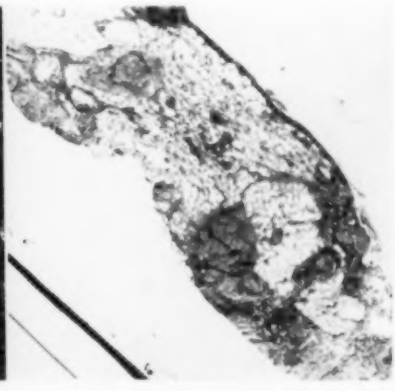

FIGURE 7

Figure 6: (Neg. 3304) Case O. S. G. Composite of the above showing areas within the hyaline collagen which contain no demonstrable mineral. Plentiful mineral dust is present in the peripheral "reactive" zone. There is also infiltration of the atelectatic alveoli by mineral aggregates.—*Figure 7:* (Neg. 3422) Case J. C. Single and coalescent silicotic nodules, some of which are laminated. Although the hyaline acellular centers have a smooth, rounded outline, they are surrounded by a cellular "reactive" zone of variable width which gives the nodules a ragged, ill-defined outline. Van Gieson-iron stain.

The earliest x-rays taken at age 50, after eight years of dust exposure, showed definite accentuation of linear marking with a fine granular infiltration in all lung fields. A small band-like density first appeared over the right apical region four years later. No significant changes were noted in films taken at the time of retirement three years later, but films taken the year of his death showed far advanced diatomite pneumoconiosis with extensive bilateral coalescent lesions in both apices and bleb formation at the bases (Figure 17).

There was a severe induration of the right upper lobe which was continuous with a similar induration extending from the hilar region along the major bronchi and vessels. A section from a region of coalescent lesions in the right upper lobe exhibits large and smaller irregular, interconnected areas of dense collagen which enclose or

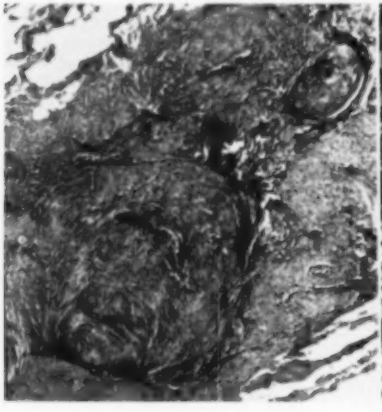

FIGURE 8

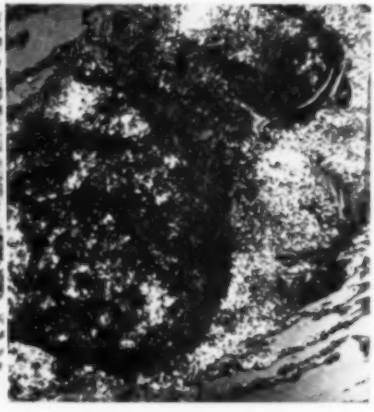

FIGURE 9

Figure 8: (Neg. 3429) Case J. C. Coalescent, smooth-contoured, laminated silicotic nodules surrounded by an irregular, cellular "reactive" zone. Partial atelectasis of adjoining alveoli. Van Gieson-iron stain.—*Figure 9:* (Neg. 3429) Case J. C. Composite of the above showing very heavy concentrations of mineral aggregates in "reactive" zone and extending into adjoining alveolar septa (lower right corner). There is relatively less mineral in the centers of the nodules.

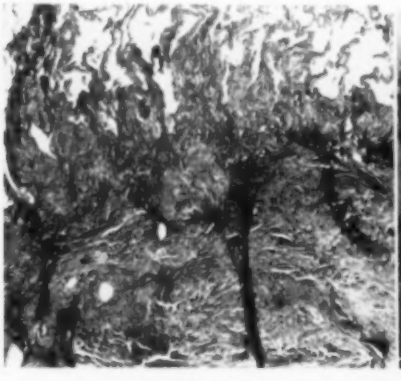

FIGURE 10

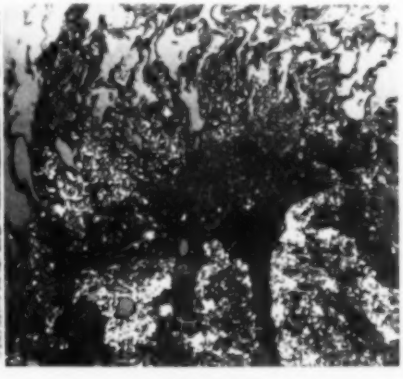

FIGURE 11

Figure 10: (Neg. 3428) Case J. C. Portion of periphery of a silicotic nodule which has sunburst appearance due to great broadening of the bases of alveolar septa. The wide dark bands cutting across the acellular collagen are folds in the section. Van Gieson-iron stain.—*Figure 11:* (Neg. 3428) Case J. C. Composite of the above showing infiltration of the radially extended thickened septa by mineral aggregates. No mineral is demonstrable in the regions of the folds, presumably because poor contact with the glass does not allow the mineral particles to be embedded in the soft surface of the glass during the incineration.

surround large vessels and bronchi as well as islands of atelectatic or emphysematous parenchyma (Figure 18). A considerable amount of iron is present. Most of this iron is not associated with silica and is situated largely at the periphery of the masses although a small amount is also found within the collagen masses and in some of the atelectatic air spaces.

The fibrous masses are largely acellular and partially hyalinized. A reactive peripheral zone of lymphocytes, monocytes and dust-laden macrophages is frequently present. The fibrous masses are associated with peri-focal atelectasis. The atelectatic alveolar walls tend, in most instances to be arranged parallel to the periphery of the nodule. Such alveolar walls are generally not thickened. But there are also club-shaped, thickened alveolar septa which tend to extend radially from a coliagenous mass and thereby give it a stellate or sunburst appearance (Figure 19). Alveolar walls generally are infiltrated by lymphocytes and monocytes.

Much of the coliagen masses is free of mineral dust but foci of dense mineral deposits are found irregularly scattered within the masses. In general, the disposition of the mineral dust is unpredictable although it is generally abundant in the reactive cellular zone on the periphery of the collagen masses. Adjacent alveolar walls, whether thickened or not, commonly are heavily infiltrated by mineral dust (Figures 20 and 22).

There is pronounced vascular sclerosis and perivascular fibrosis with narrowing of vascular lumens (Figure 21). The profuse infiltration of the perivascular tissues and, indeed, of the vessel walls themselves with mineral dust is of great interest (Figures 20 and 22).

Analysis of the dried lung tissue for mineral constitutents disclosed that the ash content was 6.98 per cent; silica, 1.62 per cent; quartz, 0.09 per cent; and crystobalite, 0.52 per cent.

5. *Asbestosis*

Case E. N., age 60, had worked for 29 years in an asbestos mill as bagger, oiler, sweeper, grader, and tester. During this time he received significant exposure to asbestos dust. The first chest x-ray film taken after 22 years of exposure indicated an advanced asbestosis. Because he was asymptomatic he remained at work and continued in his occupation without a day of sick leave for seven years longer. Shortly thereafter he rapidly became dyspneic and cyanotic. An electrocardiogram at this time was indicative of cor pulmonale. From then until his death two years later he was

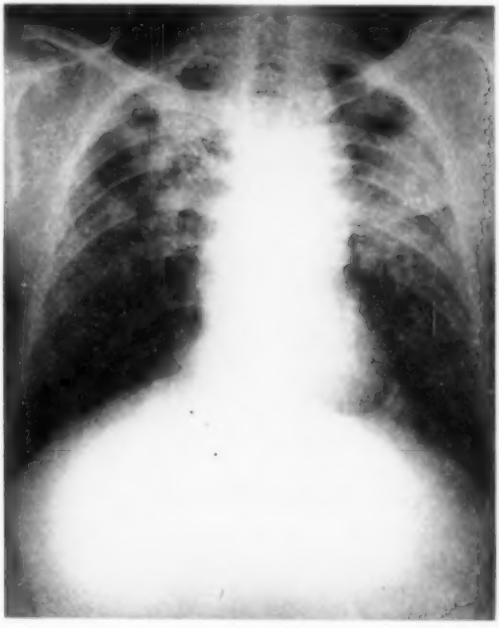

FIGURE 12: Case S. G. Advanced pneumoconiosis from inhalation of mixed dust consisting of diatomaceous earth and asbestos, complicated by tuberculosis.

totally disabled and he died with severe cardiac decompensation and generalized anasarca.

The lungs appeared enlarged and showed a greatly coarsened texture with numerous thick bands of scar tissue occurring in an increasingly prominent manner toward the lower portion of the upper lobes and still more outspokenly toward the bases. There were subpleural emphysematous spaces 2 to 4 mm. in diameter. Subpleural fibrous plaques 5 to 6 mm. in diameter were also present. The pleura was greatly thickened. Although the bronchi appeared normal, the blood vessels were appreciably thickened.

Microscopically there is irregular fibrous thickening of the parenchyma with severe distortion of the architecture (Figure 23). Few recognizable alveoli are found. Instead, there are very large, irregular, distended spaces; most of them bounded by thick fibrous septa. Larger areas of fibrosis are found in the regions of vessels and

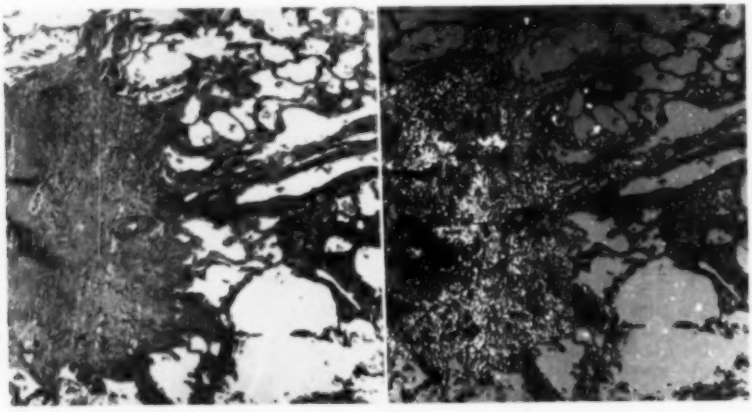

FIGURE 13 FIGURE 14

Figure 13: (Neg. 3309) Case S. G. A stellate silicotic nodule with a broad cellular reactive zone about a central acellar, hyaline focus. Van Gieson-iron stain.—*Figure 14:* (Neg. 3309) Case S. G. Composite of the above showing heavy concentration of mineral dust in broad reactive zone with infiltration of thickened radial septa by dust aggregates.

FIGURE 15 FIGURE 16

Figure 15: (Neg. 3314) Case S. G. Large, well delimited area of caseous necrosis stretching across upper portion of field and a smaller one in lower right corner. There is a silicotic nodule between these two areas of caseous necrosis. Another silicotic nodule occupies the lower left corner. Van Gieson-iron stain.—*Figure 16:* (Neg. 3314) Case S. G. Composite of the above showing complete demineralization of the areas of caseous necrosis.

bronchi, generally with considerable vascular sclerosis. Relatively little mineral dust is present in the altered parenchyma (Figures 24 and 26) and much of the scarred tissue contains no demonstrable dust. The greater part of the mineral dust appears to be non-fibrous. At high magnifications, however, scattered asbestos fibers up to 50 to 75 microns in length are seen among the crystalline plates and refractile granules.

Because no definitive information was available regarding the stability of chrysotile asbestos fibers under our conditions of incineration and acid-treatment, such data were obtained by two methods. In the first method slightly over 5 g. of finely divided chrysotile asbestos was placed into a Gooch crucible and after weighing (following a sojourn in a drying oven), incinerated at 550° C. for one hour. The crucible with its content of asbestos was then placed in a beaker containing concentrated hydrochloric acid for 30 minutes. The crucible rested on glass beads to allow for some circulation of the acid. After removal from the acid the contents of the crucible was washed with running distilled water until the wash water was chloride free (negative test with $AgNO_3$). Following drying overnight in an oven the crucible and content were weighed again. The total weight loss from this procedure was found to be only 6.3 per cent.

The second method consisted of preparing a thin smear of ultrafine asbestos dust upon a glass slide and photographing a selected field under dark field conditions before and after incineration with its subsequent acid treatment and wash. Comparison of the two pictures shows that the finest particles visible in the print before incineration are also visible in the pictures taken after the incineration and acid reatment.

Thus, we are reasonably certain that the paucity of mineral dust in our asbestotic tissue is real and not artefactual.

Discussion

Simpson and Strachan[3] differentiated between an arrested silicotic nodule and one in which the inflammation, and therefore further growth, was still progressing. The criterion for the progressiveness of a silicotic nodule, according to these writers, is the presence of a "reactive zone" on the periphery of a nodule. As seen in the present case material the reactive zone consists of lymphocytes, monocytes, fibroblasts, and dust-laden macrophages. One of the more significant findings in this study is the frequent concentration of mineral dust in the reactive zone on the periphery of a

FIGURE 17: Case E. S. Far advanced diatomite pneumoconiosis with coalescent lesions and numerous bullae.

silicotic nodule or mass and the frequent permeation of the mineral particles into the adjoining less involved or non-indurated tissues. It would appear that the presence of the high mineral dust concentration in the peripheral portion of the silicotic nodule offers a logical explanation for the existence of the reactive zone in that region and also throws light on the mechanics of the growth of the nodules.

The shape of the silicotic nodule, whether smooth or stellate, has been used by diBiasi[4] as a criterion to differentiate between nodules of pure

FIGURE 18

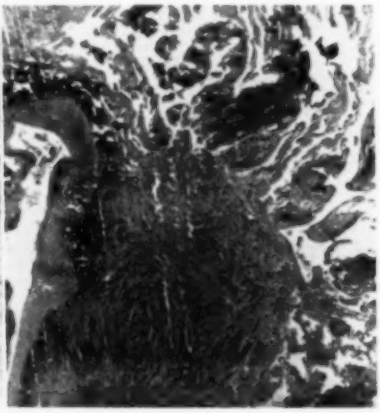

FIGURE 19

Figure 18: (Neg. 3423) Coalescent nodules and plaques of non-laminated collagen associated with many vessels of varying size most of which are sclerotic. Atelectasis and focal emphysema of nearby parenchyma. Van Gieson-iron stain.—*Figure 19:* (Neg. 3457) Case E. S. A collagenized nodule adjacent to a large vein. The reactive zone is not sharply defined. Adjoining septa are clubbed and radially arranged so as to give sunburst appearance. Van Gieson and iron stain.

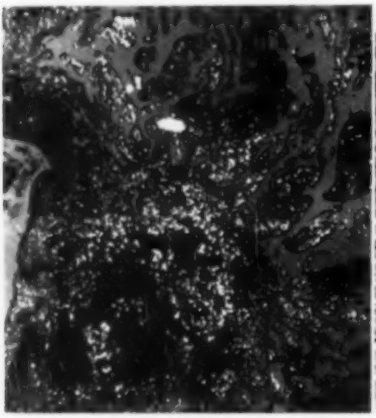

FIGURE 20

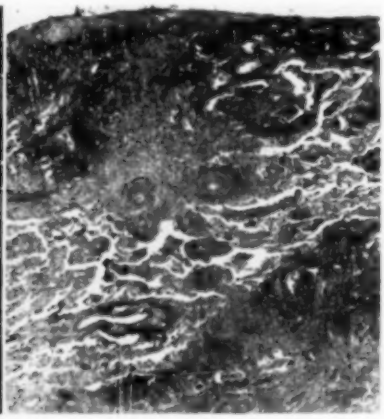

FIGURE 21

Figure 20: (Neg. 3457) Case E. S. Composite of the above showing mineral infiltration into the reactive zone, into the radiating septa, and into a portion of the vein wall.—*Figure 21:* (Neg. 3450) Case E. S. Extensive, irregular fibrosis which includes the pleura. Adjacent surviving parenchyma is atelectatic. There are a number of sclerotic arteries with narrowed lumen.

silicosis (smooth-contoured) and those of mixed silicosis. A mixture of silica with other dusts has been presumed to result in stellate nodules. Although the present study offers no data in refutation of diBiasi's contention, nevertheless the photomicrographs suggest a purely mechanical explanation for the genesis of either a smooth-contoured or a stellate nodule.

If alveolar walls at the periphery of a nodule become infiltrated with irritating mineral particles, interstitial edema followed by cellular infiltration and finally fibrosis of the structures result. Whereas initially it is turgescence which prevents collapse of the alveolar walls, later the rigidity becomes permanent by collagenization of the septa. Because the mineral infiltration is heaviest at the bases of the rigidly extended alveolar septa, the fibrosis also is greatest in this region. Thus the nodule receives a stellate or sunburst periphery.

In contrast, if the mineral particles do not infiltrate into the adjoining alveolar walls, the latter remain soft and pliable and tend to be closely applied circumferentially against the nodule by pressure of the surrounding structures. Thus the nodule retains a smooth contour.

It is highly probable that laminations in a silicotic nodule represent lines of growth and arrest. Contrariwise, the absence of laminations in a nodule suggest that its growth has been a steady one, without growth arrest. The extent to which circumferentially applied atelectatic alveolar walls also contribute to the laminated appearance of silicotic nodules must await future study. All observations to date point to a centrifugal dissemination of mineral dust in a growing silicotic nodule but it is not known at present the extent, if any, to which new silica particles from the surrounding lung tissue may contribute to the peripheral growth of a nodule.

That silicosis is a progressive disease is generally recognized. The observations recorded in the present study anent the peripheral localization

FIGURE 22

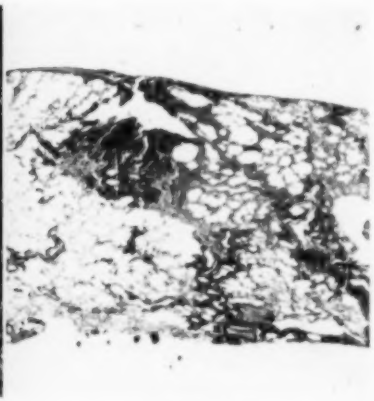

FIGURE 23

Figure 22: (Neg. 3450) Case E. S. Composite of the above. Much mineral dust diffusely infiltrates practically all tissues including those not appreciably involved by fibrosis. The thickened arteries also show mineral infiltrates in their walls. This is a picture of fulminating dissemination of mineral dust 17 years after the last dust exposure.—*Figure 23:* (Neg. 3365) Case E. N. Irregular band-like and septal fibrosis associated with severe emphysema, typical of asbestosis. Van Gieson-iron stain.

of mineral particles in the reactive zone of silicotic nodules and the tendency of these particles to infiltrate adjacent less involved or near-normal structures offer a logical explanation for this progressiveness.

It is of interest to point out that in the case of J. C. who had his last exposure to silica at age 47 and who died 25 years later at age 72 there are laminated pulmonary silicotic nodules with a reactive cellular peripheral zone (indicative of relatively recent reactivation) and dissemination of the mineral dust into adjoining tissues. Similarly, in the case of E. S. who had his last exposure to diatomite dust at age 54 and who died 17

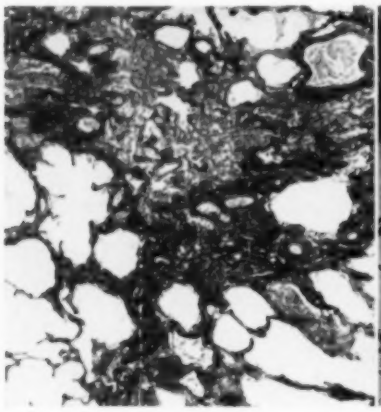

FIGURE 24

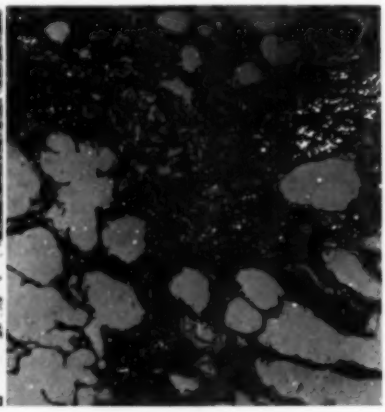

FIGURE 25

Figure 24: (Neg. 3439) Case E. N. Large, irregular scar enclosing numerous sclerotic vessels and involving adjoining alveolar septa irregularly. Van Gieson-iron stain.—*Figure 25:* (Neg. 3439) Case E. N. Composite of the above showing very little mineral in the scar tissue.

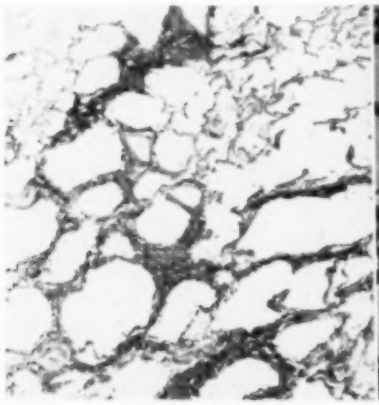

FIGURE 26

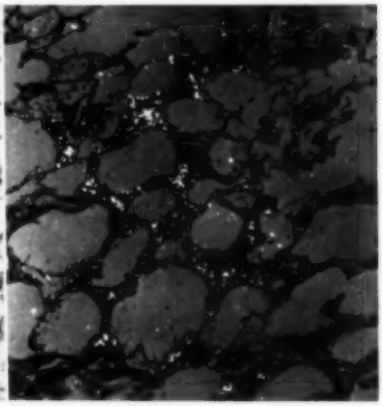

FIGURE 27

Figure 26: (Neg. 3434) Case E. N. Irregularly thickened walls of tremendously enlarged air spaces. The darkly staining foci are due to the presence of iron and asbestos bodies.—*Figure 27:* (Neg. 3434) Case E. N. Composite of the above showing little mineral dust, much of it associated with the iron. Most of the dust is in the form of granules and plates. Scattered asbestos fibers are also present.

years later at age 71, the disease at the time of death was in a state of fulminant progression as may be judged from the degree of dispersion of the mineral dust throughout the lung tissue.

In contrast to silicosis, asbestosis is not a progressive disease. Basically silicosis owes its characteristic progressiveness to the fact that silica particles deposited in one site, may be transported by tissue fluid (generally as edema fluid) to uninvolved portions of the lung to initiate new lesions.[2] Asbestos fibers, in contrast, cannot pass the intricate barrier presented by the lattice work of tissue fibers as readily as particles of the same diameter which are substantially spherical. Also, since asbestos has a very considerable solubility, dissolution of the fibers offers a plausible explanation for the paucity of mineral found in asbestotic scar tissue. Both of these factors prevent the transport of significant amounts of asbestos fibers from their site of deposition to new locations and therefore explain the non-progressiveness of asbestosis.

The absence of mineral dust from areas of tuberculous inflammation, particularly from areas of necrosis as demonstrated in Case S. G. would seem to offer a facile differentiation between a silicotic and a tuberculous nodule. To be certain of such differentiation, however, many more cases of silicotuberculosis would have to be studied in order to determine the frequency of the exception to this finding. Furthermore, it is also well to consider that some silicotic nodules may be almost completely demineralized in the absence of an associated tuberculous inflammation.

Vascular sclerosis is seen frequently in silicosis,[5] and seems to be especially pronounced in case E. S. in which cristobalite is the most important fibrogenic agent. The striking feature of this case is the extensive infiltration of mineral particles into the walls of the diseased vessels, a phenomenon not previously observed in any other pneumoconiosis. Zaidi et al[6] have demonstrated the greater fibrogenic potential of cristobalite over quartz but whether or not the infiltration of vessel walls by mineral dust is a characteristic feature of cristobalite pneumoconiosis can only be decided by further study.

SUMMARY

By means of a photographic method it has been possible to study the topographic distribution of otherwise occult mineral dust deposits in the lungs. The more important features of mineral dust distribution in several types of silicosis as well as of asbestosis are described and illustrated.

The progressive character of silicosis is explained on the basis of the transport of silica from the site of deposition to new locations where fresh inflammatory reactions are initiated. Such transport is demonstrated in ancient hyaline nodules which exhibit a peripheral "reactive" zone of younger, cellular inflammatory tissue in which mineral dust particles are heavily concentrated. Another striking indication of how the transport of mineral dust may lead to the development of new inflammatory foci is seen in the demonstration of heavy mineral dust infiltrations into uninvolved parenchyma adjacent to silica nodules.

The non-progressive character of asbestosis is explained by the paucity of demonstrable mineral in asbestotic scar tissue and by the difficulty of mobilizing and transporting asbestos fibers through the impeding lattice work of stromal fibrils.

The significance of rounded versus stellate, and of laminated versus non-laminated silicotic nodules is discussed in the light of the present observations and demonstrations.

Areas of tuberculous inflammation, particularly of caseous necrosis, though occurring in the midst of silicotic tissue are shown to be free of demonstrable mineral dust particles.

An example of the cristobalite type of silicosis is shown to possess a fulminating progressiveness 17 years after the last exposure to this dust. An interesting side light to this disease is the demonstration of mineral dust infiltrating vessel walls.

Acknowledgements: The writers wish to thank Dr. Paul Cartier of Thetford Mines, Canada for allowing us to use case E. N. and Dr. E. L. Schafer of Madison, Wisc., for the use of case J. C. We are also indebted to Dr. William H. Carnes of Salt Lake City, Utah for significant data used in case E. S. To Miss Ethel Tolker, M.S., M.T. (A.S.C.P.) the writers express their appreciation for her efforts and meticulous care in the preparation of these difficult sections.

RESUMEN

Por un procedimiento fotográfico ha sido posible estudiar la distribución topográfica de depósitos de polvos minerales que de otra manera permanecerían ocultos. Se ilustra la distribución característica de polvos minerales en los tipos diversos de silicosis y de asbestosis.

El carácter progresivo de la silicosis, se explica sobre la base del transporte de sílice desde el lugar de depósito inicial hacia nuevos sitios donde se inician reacciones inflamatorias nuevas. Ese transporte se demuestra por antiguos nódulos hialinos que muestran una zona periférica "reactiva" de tejido más joven inflamatorio en la que se han concentrado partículas minerales en gran proporción.

Otra notable indicación de cómo el polvo mineral transportado puede conducir a la creación de nuevos focos inflamatorios se ve en la demostración de grandes infiltraciones de polvo mineral hacia tejido no comprometido adyacente a los nódulos de sílice.

El carácter no progresivo de la asbestosis se explica por la escasez de mineral demonstrable en el tejido cicatricial de asbestosis y por la dificultad de movilizar y transportar las fibras de asbestos a través de las mayas que dificultan esto y a través de las fibrillas del estroma.

A la luz de las observaciones actuales se discute la significación de los nódulos redondos contra estelares y laminados versus no laminados.

Las áreas de inflamación tuberculosa, particularmente de necrosis caseosa, aunque ocurren enmedio de tejido silicótico se demuestra que están libres de polvo mineral. Un ejemplo del tipo de silicosis llamada "cristobalito" se demuestra que posee una evolutividad progresiva 17 años después de la última exposición al polvo de sílice. Una interesante demostración colateral de esta enfermedad es la presencia de polvo de mineral infiltrando las paredes de los vasos.

RESUME

Il été possible d'étudier par photographie la distribution topographique des dépôts occultes de poussière minérale dans les poumons. Les auteurs décrivent les aspects les plus caractéristiques et les modalités les plus im-

portantes de distribution des poussières minérales dans différents types de silicose et d'asbestose.

Le caractère progressif de la silicose s'explique par la migration de la silice de son point de dépôt vers les localisations nouvelles où paraissent des réactions inflammatoires récentes. Cette migration est démonstrée dans les anciens nodules hyalins, oú existe une zone periphérique "réactionnelle" de tissu inflammatoire cellulaire jeune, dans lequel les particules de poussière minérale sont fortement concentrées. Une autre démonstration frappante de la migration de la poussière minérale est offerte par le développement de nouveaux foyers inflammatoires avec infiltrations importantes de poussière minérale dans une zone du parenchyme jusqu'alors non atteinte et adjacente aux nodules de silice.

Le caractère non évolutif de l'asbestose est expliqué par le peu de minéral mis en évidence dans le tissu cicatriciel asbestosique et par la difficulté du cheminement et du transport des fiberes asbestosiques à travers les lacets obstructifs des fibrilles du stroma.

Les auteurs discutent la signification des nodules silicotiques arrondis par rapport à ceux qui sont étoilées, et de ceux qui sont lamines par rapport à ceux qui ne le sont pas, en fonction, des remarques et les démonstrations qu'ils viennent de présenter.

Les zones d'inflammation tuberculeuse, particulièrement la nécrose caséeuse, bien que survenant au milieu de tissu silicotique, ne contiennent aucune particule de poussière minérale visible.

Un cas de silicose cristobalite se présenta avec un potentiel évolutif foudroyant 17 ans après la dernière exposition à ces poussières. Un autre point intéressant de cette affection est l'existence de poussière minérale infiltrant les parois vasculaires.

ZUSAMMENFASSUNG

Unter Zuhilfenahme eines photographischen Verfahrens war es möglich, die topographische Verteilung von sonst verborgenen Mineralstaub-ablagerungen in den Lungen zu untersuchen. Beschreibung und Illustrierung der wichtigeren Eigentümlichkeiten der Verteilung von Mineralstaub bei verschiedenen Typen von Silikose sowohl als auch von Asbestose.

Der fortschreitende Charakter der Silikose wird gedeutet auf der Basis des Transportes von Silicium von der Stelle der Ablagerung zu neuen Lokalisationen, wo frische entzündliche Reaktionen hervorgerufen werden. Ein solcher Transport wird demonstriert an alten hyalinen Knoten, die eine periphere "reaktive" Zone jüngeren, zellulären entzündlichen Gewebes hervorbringen, in der Mineralstaubteilchen grob konzentriert sind. Ein anderes eindrucksvolles Merkmal dafür, auf welche Weise der Transport von Mineralstaub zur Entwicklung neuer entzündlicher Herde führen kann, lässt sich erkennen an dem Nachweis der beträchtlichen Mineralstaub-Infiltrationen in die nicht befallenen Gewebsabschnitte in der Nachbarschaft von silikotischen Knoten.

Der nicht fortschreitende Charakter der Asbestose wird erklärt durch die geringe Zahl von nachweisbarem Mineral in asbestotischem Narbengewebe und durch die Schwierigkeit, Asbestfasern zu mobilisieren und zu transportieren durch das störende Gitterwerk der Grundgewebsfibrillen.

Besprechung der Bedeutung von abgerundeten gegenüber sternförmigen und von lamellenförmigen gegenüber nichtlamellenförmigen Silikoseknötchen im Lichte der vorgelegten Beobachtung und Demonstration. Es wird gezeigt, dass Bezirke mit tuberkulöser Entzündung, ganz besonders mit käsiger Nekrose, auch wenn sie mitten in silikotischem Gewebe vorkommt, frei sind von nachweisbaren Mineralstaubteilchen.

An einem Beispiel des Silikosetyps von CRISTOBAL wird gezeigt, dass er eine plötzlich ausbrechende Progredienz aufweist 17 Jahre nach der letzten Silikosestaub-Exposition. Einen bemerkenswerten Seitenblick wirft auf diese Erkrankung der Nachweis von mit Mineralstaub infiltrierten Gefässwänden.

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Mass Tuberculin Patch Testing of School Children (A Critical Analysis of 125,000 Cases)*

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During the past four years the St. Louis Academy of General Practice has engaged in a community case finding program in tuberculosis in cooperation with the St. Louis Tuberculosis and Health Society and the St. Louis County Health Department. Details of the history and development of this program including complete description of its operation and organization can be found in articles in the JAMA[1] and The Journal-LANCET.[2] Reprints of these articles as well as a silent motion picture in color are available on request to those who might be interested in such a program.

Attesting to the interest shown in this program is Table I showing its growth since 1950. It will be noticed that the program did not gain momentum until 1953 at which time the three organizations involved joined forces to initiate a community wide effort as the result of a pilot program sponsored by the St. Louis Academy of General Practice in the Ritenour School District.

By the end of 1955, 111,602 school children had been patch tested with an overall positive reactor rate of approximately 5 per cent giving a total number of 5,580 positive reactors. Although complete figures are not yet available relating to the exact number of contacts x-rayed for each positive reactor a very close estimate would be 15,000 reactors and contacts x-rayed as the result of this program. Of this number 41 persons were found to have active tuberculosis previously undiscovered. Table II illustrates the relationship.

To further point out the effectiveness of the patch test program, not only as a screening device but also as a case finding method, the following comparison is taken from the period 1953-1955 showing how positive patch tests can pin-point pathology.

This has become the watchword of our program "POSITIVE PATCH TESTS PIN-POINT PATHOLOGY." We have coined another slogan which reads as follows "ELIMINATION OF NON-REACTORS AND EDUCATION OF POSITIVE REACTORS EFFECTS ECONOMY." To illustrate this let us consider the following. For several years the Tuberculosis and Health Society of St. Louis has carried on a program of mass x-rays of Juniors and Seniors in St. Louis County High Schools. In the two year period 1953-1955, 24,316 students and school personnel were x-rayed at the cost of approximately $24,000. As a result of this program one active case was found per 24,316 x-rays. During a similar period (1954-1956) 64,317 patch tests were applied in the St. Louis County grade schools and high schools. As a result of this 9,998 positive reactors and contacts were x-rayed resulting in the discovery of 15 new active cases of tuberculosis,

*Presented at the 23rd Annual Meeting, American College of Chest Physicians, New York City, May 29-June 2, 1957.

TABLE I
NUMBER OF PATCH TESTS APPLIED BY VARIOUS AGENCIES
(ALL FIGURES ARE CUMULATIVE)

Year	City Schools	County Contract St. Louis Health Dept.	St. Louis Academy of G.P.	Independent
1950	139			
1951	2,389			220
1952	3,941	4,419		2,035
1953	5,524	15,603	11,689	4,031
1954	10,564	24,277	26,092	4,031
1955	15,962	39,453	50,171	6,016

TABLE II

Number of Patch Tests	111,602
Positive Reactors and Contacts X-rayed	15,000
Active Cases, Reactors (Schoolchildren)	16
Contacts (Adult)	25

TABLE III

Patch Test 1953-1955		Survey 1953-1955	
	Screening		
Number of patches	50,275	Number of small x-rays	125,161
Number of active cases	16	Number of active cases	53
Number x-rays positive reactors and contacts	4,866		
Number small x-rays for each active case	293 (0.3%)	Number small x-rays for each active case	2,362 (0.04%)

TABLE IV

Year	Type of Program	No. of Patch Tests	No. of X-Rays	New Active Cases	
1953-55	County school x-rays Surveys (11th & 12th Grades and School Personnel)	0	24,316	1	1 active case found per 24,316 x-rays.
1954-56	County Patch test Program (Grades 1 through 12)	64,317	9,998	15	1 active case found per 667 x-rays 1 active case found per 4,288 patches.

or one active case per 667 x-rays, or one active case per 4,288 patch tests. Table IV graphically illustrates the effectiveness of the patch test program as a screening method and also shows obvious differences in expenditures for x-rays in the two programs.

Sooner or later we must come to the question which invariably arises in a discussion of tuberculin patch testing. Someone is bound to question the accuracy of the patch test as compared to the Intradermal or Mantoux test. We are the first to admit that the patch test cannot possibly be as accurate as the Mantoux test. As of May 1957, 144,912 patch tests have been applied in connection with this program. We have experienced all the difficulties inherent in faulty adhesive qualities especially during early Fall and late Spring programs. However we feel that an over-all consent rate of 95 per cent in schools where we have carried out this program more than offsets the difference in accuracy since it is our feeling that consent would drop off sharply if we attempted the Intradermal test in the same schools. We would like to do a control series using both patch tests and Mantoux tests in the same group but it has taken too long to evolve a smoothly running program to jeopardize it at this stage. If there is anyone interested in doing a comparable number of Mantoux tests under conditions similar to our patch test program we shall be glad to give the utmost cooperation in compiling statistics for such a joint endeavor.

Probably one of the most interesting and valuable aspects of our community case finding program is the health education program that has evolved with it. Under the close direction of Miss Ellen Boyce, the Executive Secretary of the St. Louis Tuberculosis and Health Society, and President of the National Conference of Tuberculosis Workers, Mrs. Alice Mason, local Director of the Tuberculin Patch Testing Section along with Miss Daisy Jacobs, local Director of Health Education, have developed a close knit, effective educational program which has paid tremendous dividends in public relations and health education. Through this program, before a child is patch tested, the faculty, the parents, and the children themselves have been orientated by visual means, through motion pictures, posters and pamphlets and also by lectures and talks to faculty groups, P.T.A. meetings and student assemblies. In the lower grades children are reached on a room to room basis by individual health education workers. The growth of this aspect of the program is illustrated by Table V. (Please note that all figures are cumulative.)

Three years ago we adopted an orphan program and had a difficult time selling it to local school boards. As a result of the health education program our patch test program has had to be frozen each year by February

TABLE V
HEALTH EDUCATION PATCH TESTING PROGRAM

	1950-51	1951-52	1952-53	1953-54	1954-55	1955-56	Cumulative
Schools	3	8	23	73	96	182	385
Meetings	7	47	59	367	409	470	1,359
Films	6	47	59	111	157	239	613
Talks	7	47	59	367	409	470	1,359
Attendance	313	3,879	4,897	22,655	32,768	36,288	100,802

or March during the past two years and also for the coming year. This year we will add approximately 12,000 new children to the program which represents a backlog of requests during the last 18 months.

At present the Academy follows the procedure of testing the entire school population during the initial program; thereafter doing a yearly spot check program involving the first, fifth and ninth grades plus newcomers. In addition to that the Academy also continues to patch test the entire population of the 11th and 12th grades in high schools involved in the program. The County Health Department continues to patch test the entire school population of their contract schools on a yearly basis. This difference is due primarily to a difference in available volunteer manpower of the Academy compared with an organized stable number of paid personnel available to the County Health Department. Dr. John C. Murphy, who is in charge of the County Health Department program, has always given wonderful cooperation and now that he has an IBM card system established for closer follow-up of positive reactors and contacts, his part in the program will assume an ever-increasing importance.

There is one other aspect of this program I should like to discuss to show the value of a patch test program as a screening method. The first real attempt at mass testing of school children was carried on in the Ritenour School District early in 1953. The fact that five parents with active tuberculosis were discovered and placed under treatment as a result of patch tests on less than 5,000 school children gave tremendous impetus to the development of our present procedure. Later programs, however, did not bear such a high yield and after a year or so it was assumed that we had unwittingly stumbled on a high incidence area of tuberculosis in St. Louis County. About one year later when we were having difficulty budgeting x-rays in the over-all City and County mass x-ray survey program it was decided to test that theory in a practical manner. To obtain the needed films for a community type survey the Academy of General Practice and the St. Louis County Health Department agreed to replace the x-ray program in St. Louis County High Schools with a patch test program, thereby releasing some 8,000 70 mm. films to be used by the Tuberculosis and Health Society in the Ritenour Community survey. The County Health Department also agreed to furnish additional films to aid in this survey. While final tabulations are not available we do know that there is a higher incidence of active cases found per thousand 70 mm. films in the Ritenour area than there is in St. Louis County as a whole, illustrating once more, and finally, "POSITIVE PATCH TESTS PINPOINT PATHOLOGY."

(It was hoped that all statistics would be available on the basis of 125,000 patch tests. Unfortunately the untimely illness and subsequent death of our Statistician's husband, resulting in her leave of absence for a prolonged period, leaves us considerably behind schedule in sifting statistical material suitable for publication.)

SUMMARY

Incomplete statistics on the first 111,000 tuberculin patch tests show an over-all positive reactor rate of approximately 5 per cent.

Approximately 15,000 reactors and contacts examined including x-ray

films of Chest produced 41 new cases among reactors and adult contacts, 16 school children and 25 adults.

Comparison of programs using the patch test as a screening procedure with mass x-ray film surveys show a case finding rate per 100 small x-ray films taken to be approximately 10 times that using the mass x-ray film survey program alone. In county school x-ray film surveys of the 11th and 12th grades one active case was found per 24,316 films. In county schools, grades one through 12, using the patch test as a screening procedure, one active case was found per 667 films or one active case per 4,288 patches.

Health education is one of the primary objectives of the program in addition to tuberculosis case finding. Attendance at meetings in connection with this program has grown from 313 to 36,288. These are yearly totals for 1950-51. In 1955-56 the cumulative total is 100,802 persons attending such meetings over a six-year period.

It is to be emphasized that this is a co-operative community venture, sponsored by the St. Louis Academy of General Practice in co-operation with the Tuberculosis and Health Society of St. Louis and the St. Louis County Health Department.

Attention is drawn to the fact that while the patch test is admittedly not as accurate as the intradermal or Mantoux test, still it is admirably suited to a controlled group such as school children; and that our case finding rate over the past five years has more than justified the existence of the program.

RESUMEN

La estadística incompleta de las primeras 111,000 reacciones tuberculínicas de parche, mostraron en general una proporción de 5 por ciento de reactores positivos.

Aproximadamente 15,000 reactores y contactos examinados incluyendo películas de rayos X, produjeron 41 nuevos casos entre reactores y contactos adultos, 16 niños de escuelas y 25 adultos.

La comparación de planes que usan el parche como procedimiento de detección con roentgenfotografía de masas, muestra una proporción de descubrimiento de casos diez veces mayor que usando sólo la roentgenfotografía. En las escuelas del condado las investigaciones por roentgenfotografía de los grados 11° y 12°, dieron un caso activo por 24,316 roentgenfotografías. En las escuelas del condado en los grados desde uno al 12°, usando la prueba del parche, se encontro un caso activo per 667 películas de roentgenfotografía, o un caso activo por 4,288 parches.

La educación sanitaria es uno de los objetivos primordiales del plan además del hallazgo de casos. La asistencia a las reuniones en relación con este programa, ha aumentado de 113 36,288. Estos son totales anuales para 1950-1951. En 1955-1956 el total acumulado es de 100,802 personas que han asistido a esas reuniones por más de seis años.

Hay que recalcar que ésta es una empresa cooperativa de la comunidad respaldada por la Academia de Práctica General de San Luis en cooperación con la Sociedad de Salubridad y de Tuberculosis de San Luis y del Departamento de Salubridad del Condado de San Luis.

Se llama la atención sobre el hecho de que si bien el método del parche se admite que no es tan efflacto como el intradérmico o de Mantoux, aún así es admirablemente adecuado para un grupo controlado como el de escolares; y que la proporción de hallazgos en los 5 años pasados ha justificado con exceso la existencia del plan.

RESUME

Des statistiques incomplètes portant sur les premiers 111.000 tests cutanés à la tuberculine (patch test) montrent un taux moyen de réactions positixes d'environ 5%.

A peu près 15.000 réactions et contrôles comprenant les films radiologiques des poumons, mirent en évidence 41 nouveaux cas de tuberculose parmi les allergilquses et les individus en contact soit 16 enfants d'âge scolaire et 25 adultes.

La comparaison des campagnes utilisant le timbre tuberculinique comme moyen de contrôle associé aux examens radiologiques systématiques montre un taux de dépistage pour 100 petits films radiologiques approximativement 10 fois supérieur au procédé utilisant seulement l'examen radiologique systématique. Dans les examens systématiques de la population scolaire du district, concernant les classes de 2° et Ière, on trouva un cas actif de tuberculose sur 24.316 films. Dans les écoles du district, de la 12ème à la Ière, en utilisant le timbre comme moyen de contrôle, on trouva un cas actif pour 667 clichés ou un cas actif pour 4.288 tests tuberculiniques.

Outre le dépistage de la tuberculose, l'éducation sanitaire est un des premiers objectifs de la campagne. Le nombre des personnes assistant aux réunions de cette campagne a progressé de 313 à 36.288, (totaux annuels pour 1950 et 1951). En 1955-56, le total des personnes ayant assisté à ces réunions pendant une période de six ans est de 100.802.

On doit signaler que cette campagne a été une entreprise collective, parrainée par l'Académie St-Louis de Médecine Générale, en collaboration avec la Société de la Tuberculose et d'Hygiène de St-Louis et le Service de Santé du District de St-Louis.

On doit attirer l'attention sur le fait que, bien que l'on admette généralement que le "timbre" soit moins fidèle que le test intradermique ou test de Mantoux, il convient admirablement à un groupe surveillé tel que cel ui des enfants d'âge scolaire; notre taux de dépistage, portant sur les cinq dernières années, a plus que justifié l'existence de notre programme d'action.

ZUSAMMENFASSUNG

Unvollständige Statistiken der ersten 111,000 Tuberkulin-Pflasterproben zeigen eine Gesamtrate positiv reagierender Fälle von ungefähr 5%. Die Untersuchung von ungtfähr 15,000 positiv reagierenden Fällen und Kontaktfällen unter Einbeziehung von Thorax-Röntgenaufnahmen ergab 41 neue Fälle unter den positiv reagierenden und Erwachsenen Kontaktfällen, nämlich 16 Schulkinder und 25 Erwachsene. Ein Vergleich des Vorgehens mit Benutzung der Pflasterprobe als Suchverfahren und der Röntgen-Reihenuntersuchung ergeben eine Rate gefundener Fälle, bezogn auf 100 Schirmbilder die ungefähr das 10 fache derjenigen be-

trägt, die ausschliesslich der Röntgen-Reihenuntersuchungen verwendet. Bei Schirmbilduntersuchungen von 11. und 12. Kreisschulklassen wurde ein aktiver Fall ermittelt pro 24,316 Röntgenaufnahmen. Unter Verwendung der Pflasterprobe als Suchverfahren wurde in Kreisschulen von der 1. bis zur 12. 2Klasse ein aktiver Fall ermittelt auf 667 Röntgenfilmen oder ein aktiver Fall auf 4,288 Pflasterproben.

Erziehung zu gesundem Leben ist eines der ersten Ziele des Planes zusätzlich zur Tuberkulose-Fallsuche. Teilnahme an Veranstaltungen in Verbindung mit diesem Plan hat zugenommen von 313 auf 36,288. Dies sind die jährlichen Gesamtzahlen für die Zeit von 1950-1951. Für die Jahre 1955-1956 beträgt die addierte Gesamtzahl 100,802 Personen, die im Verlauf von 6 Jahren solche Veranstaltungen besuchten. Es muss hervorgehoben werden, dass es sich hierbei um einen kommunalen gemeinschaftlichen Einsatz handelt unter der Fördrung der Akademie für Allgemeinpraxis von St. Louis in Zusammenarbeit mit der Tuberkulose- und Gesundheits-Organisation von St. Louis und mit der Kreisgesundheitsabteilung von St. Louis.

Es wird die Aufmerksamkeit gelenkt auf die Tatsache, dass die Pflasterprobe, auch wenn sie als nicht so genau gilt wie die intrakutane oder Mantoux-Probe, doch bewundernswert für eine beschränkte Bevölkerungsgruppe passt, wie es Schulkinder sind, und dass unsere Zahl gefundener Fälle während der letzten 5 Jahre das Bestehen des Programmes mehr als gerechtfertigt hat.

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A Preliminary Report on the Radiologic Evaluation of Trypsin in Certain Chronic Chest Diseases

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The proteolytic enzyme, trypsin, is finding a broad range of uses in medicine. It has been found to increase permeability of tissues which are partially obstructed by inflammation or perhaps by cellular debris. Other observers have reported, and our findings lend confirmatory support to the thesis, that trypsin increases the liquefaction of thick mucus. Laboratory work has demonstrated[1] that the enzyme decreases the degree of inflammatory change around an intentionally traumatized area and tends to resolve the viscid accumulations of edema fluid surrounding the injury. Microscopic examination of inflammatory masses demonstrated a diminution of the fibrin, platelet, and cellular substances, in trypsin-treated animals compared to controls.[2]

In our previous work,[3, 4] clinical changes have been reported following the administration of trypsin to patients with certain chronic chest diseases. In those conditions where tenacious, inspissated mucus had impaired breathing, daily intramuscular injections of the enzyme appeared to lessen the viscosity and tenacity of the sputum, facilitating the raising of this embarrassing and inconveniencing "gunk." Subsequently, the volume of the expectorate decreased and breathing became easier. Subjective effects were noted uniformly. In addition, objective studies were undertaken in the patients and the results were confirmatory, but not as consistent as the subjective improvement.

Methods and Materials

Radiologic examinations were made on all patients before and after a course of trypsin treatment. Some measure of difference was seen in almost all patients, and in half of them the degree of improvement was classed as marked.

The purpose of this paper is to present the x-ray findings, as offered by the consulting roentgenologist who took the x-ray films, and also to present the readings of a reviewing roentgenologist. It has been shown convincingly by teams of experienced radiologists[5, 6] studying chest films of tuberculous patients that correlation between observers, and indeed duplicate readings by the same observer, are difficult to attain, particularly on borderline cases. Changes occurring in serial x-ray film studies of patients with varied chest diseases can be equally as confusing. In a personal communication from Chamberlain,[7] the point was discussed and somewhat clarified, especially as regards this study. He mentioned that he had been conducting studies for the past 15 years with a group of radiologists and chest specialists on the personal equation and the interpretation of roent-

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genograms. For the last six years, serial chest films have been studied and the group has learned how often mistakes were made when they have attempted to evaluate minor differences in x-ray film appearance. Technical factors, such as a slight shift in position of the focal spot, can change the appearance of a chest film, even when exposures are identical. He warned that it is extremely hazardous to render an opinion that a change has taken place in the pathologic condition of the lungs unless the evidence is unequivocal.

Roentgenograms of six cases, in which improvement was reported, were submitted for review to an impartial observer. These then were read without prior reference to the roentgenologist's reports. In three cases the reviewing observer was convinced that there was no x-ray evidence of improvement when the serial films were compared with each other. In the remaining three cases the evidence was considered "quite definite, reliable and convincing."

Reproductions of these films and the reports are presented.

All patients in the series, including the three represented here, received trypsin, 5 mg. once daily for a week, then three to eight injections tapered over the next two or three weeks. X-ray films were taken before treatment, again after 10 to 14 days, and in some again after six to eight weeks. In each instance a positive diagnosis was established by diagnostic allergic methods. Associated chest pathology included chronic emphysema, chronic bronchitis, and bronchiectasis. Inability to raise inspissated mucus was a requisite for inclusion in the series.

Case 1: D. C., is a white woman, age 64 who had chronic bronchitis, for 10 years and severe bronchial asthma for five months. She had severe coughing, and choking spells and breathing with difficulty. X-ray film impression was partial atelectasis, infection and pneumonitis, or extensive bronchiectasis. She was relieved of asthma in four days.

The Consulting Radiologist's Report:

January 3: The rib cage is symmetrically developed and normal. The whole of the left base up to approximately the third rib anteriorly is occupied by linear and mottled densities merging with the heart and obscuring most of the lung detail in the left base. The left upper lung field is clear. There are many linear densities in the right base due to markedly thickened and prominent bronchovascular markings. The diaphragms are sharply outlined and the costophrenic angles are clear.

January 13: There is a dramatic improvement in the left base which previously had the appearance of a partial atelectasis with many linear and mottled densities which were dense enough to obscure the left border of the heart. At this examination, the left lung field is entirely clear. The emphysema and moderate peribronchial fibrosis remain.

April 13: There is still further improvement in the bronchovascular markings of the left base, which at this reading are practically within normal limits.

The Reviewing Radiologist's Report:

The first of the three films shows a tremendous amount of actual pneumonitis in the left lung involving the lingula of the left upper lobe as well as the lower lobe. There are less extensive inflammatory changes in the right middle and right lower lobes; how much of the abnormal density in the right base is due to pneumonitis and how much to congestion is

questionable. The heart silhouette at the left border is almost entirely destroyed, the heart being in contact with non-aerated lung. Underexposure, at least partially due to the heavy breast shadow, has cut the amount of x-ray down to the point where significance of the dim silhouette of the left leaf of the diaphragm is questionable.

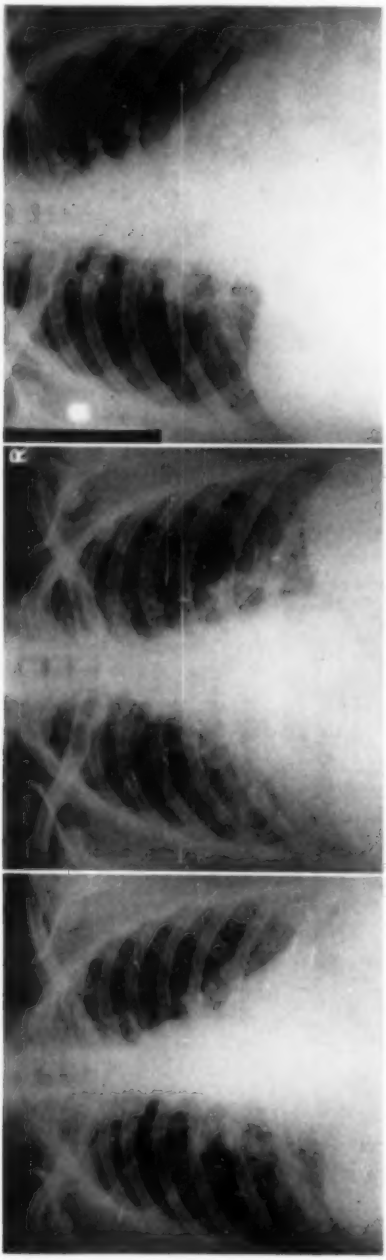

FIGURE 3

FIGURE 2 (CASE 1)

FIGURE 1

The January 13th film shows a definite improvement in the silhouette of the left border of the heart shadow, and the April 13th film shows the same improvement. The left leaf of the diaphragm is poorly shown in all three films, which may be due to the technical factors described above.

There appears to be a very marked improvement between the January third and January 13th films, with some question as to whether there was additional improvement afterwards. There is a definite difference in respiratory phase, and the diaphragm is crowded upward at the time of the January 13th exposure.

Case 2: L. C. is a white man, age 26 who has had asthma for 18 years. He has tried many physicians and many climates with no relief. X-ray film impression: marked peribronchial and pulmonary fibrosis. Profuse raising dwindling to least amount he can remember during course of treatment. Says he feels better than he can remember.

The Consulting Radiologist's Report:

November 6, 1954: The rib cage is symmetrically developed with some widening of the interspaces. The hilar regions are markedly increased in width and density and the bronchovascular markings are extremely prominent, particularly throughout both midlung fields, extending to both infraclavicular regions. The lungs are also moderately hyperaerated but the fields are essentially clear. The diaphragms are low, but sharply outlined, and the costophrenic angles are clear.

November 30, 1954: A marked improvement in the density of the bronchovascular markings, particularly in the infraclavicular regions. The left lung field, although emphysematous, is clear and shows a dramatic improvement. There is also a generalized decrease of all the bronchovascular markings, although of course they are still prominent.

April 11, 1955: Further improvement in the decrease of the bronchovascular markings particularly noticeable in the right infraclavicular region. At the present examination, except for a moderate emphysema and a slight increase in the bronchovascular markings in the right lower lung field, the chest is within fairly normal limits.

The Reviewing Radiologist's Report:

There is a marked abnormal density in the hilar regions of the November 1954 film, with a considerable degree of improvement in the x-ray film appearance when the two November films are compared with each other. The demonstration is interfered with to some extent by the marked difference in exposure density. In spite of the technical disparity, there is no question that some improvement has occurred, particularly in the part of the lung field which is in the cardiohepatic angle at the right base. Here there has been improvement in the diaphragmatic silhouette and cardiac silhouette in addition to the definite increase in the aeration of the lung and decrease in the dimensions and the density of the lung detail. The April film shows further evidence of improvement, particularly at the left base near the apex of the heart, and most particularly at the lung roots, which show a very different configuration and marked difference in size when compared to the November films.

Case 3: M. C. is a white woman, age 25 with asthma of nine year's duration. She had been hospitalized many times and treated in many clinics. X-ray impression: advanced emphysema and marked peribronchial fibrosis. After a week of treatment was remarkably improved and raising freely.

The Consulting Radiologist's Report:

November 1, 1954: There is marked widening of the interspaces. The lungs throughout are extremely hyperaerated and emphysematous, particularly in the left upper lung field. The fields, however, are essentially clear. The hilar regions are markedly increased in width and density and

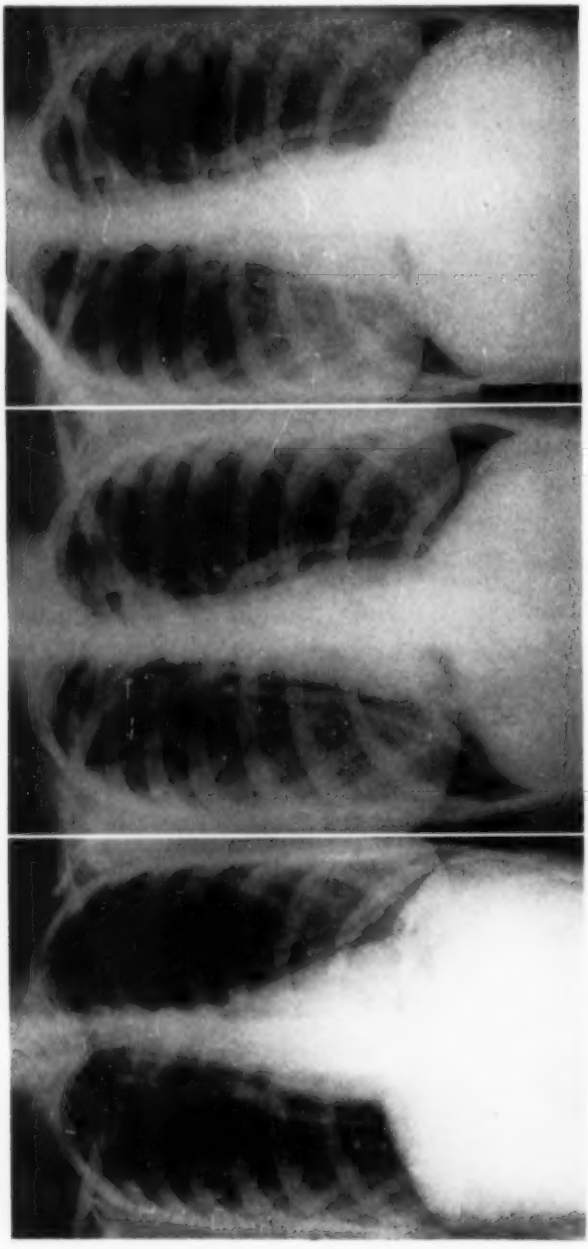

FIGURE 3

FIGURE 2 (CASE 2)

FIGURE 1

all of the bronchovascular markings are extremely exaggerated, the terminal branches being widened by the emphysematous alveoli, particularly in the left midlung field and left base. The diaphragms are low but sharply outlined and the costophrenic angles are clear. The heart and superior mediastinal shadow are not remarkable.

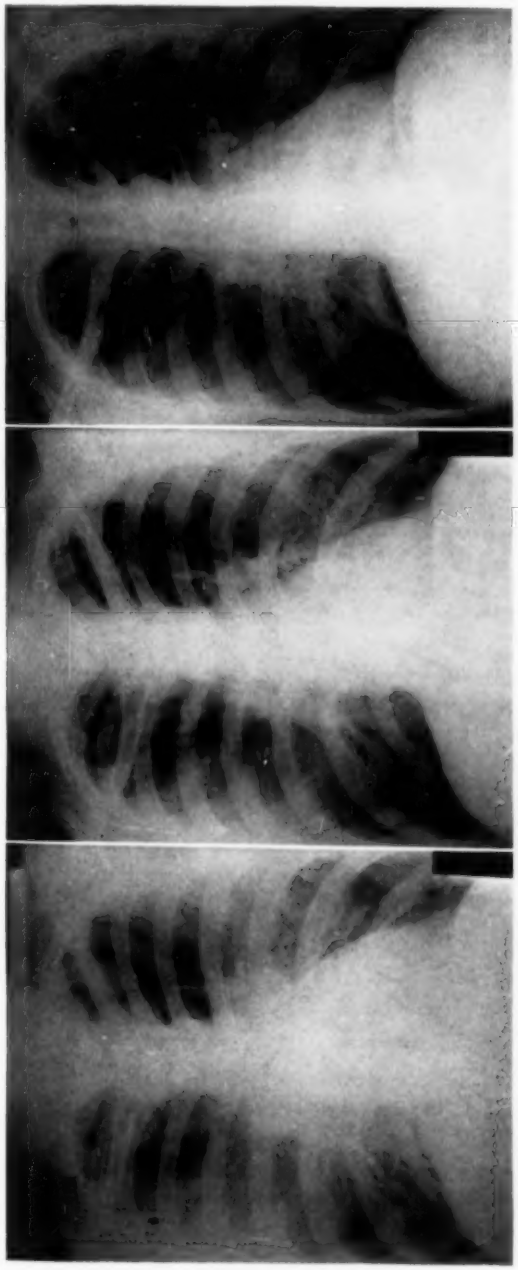

FIGURE 3

FIGURE 2 (CASE 3)

FIGURE 1

November 15, 1954: The lungs are still hyperaerated and emphysematous with the fields essentially clear. There is a definite reduction of the density of the bronchovascular markings, especially in the left base. Very little change is observed in the right base.

April 11, 1955: The bronchovascular markings have returned pretty much to the first film taken on November first, whereas the second examination showed slight improvement in the left base.

The Reviewing Radiologist's Report:

In all three films the upper ⅓ of each lung field is entirely within normal limits. There is a scoliosis in the upper thoracic spine area which has to be taken into consideration in explaining the x-ray appearance in the caudal portions of both lung fields. The films of November first and 15th show some significant changes. Hazy increases of density are in the lung fields, and the silhouettes of the right and left leaves of the diaphragm are interfered with, indicating contact with pneumonic or atelectatic lung instead of normal aerated lung. The November 15th film shows definite improvement: some of the patches of abnormal density have cleared and there has been some improvement in the visualization of the silhouette of the diaphragm, indicating a clearing of the inflammatory process at both bases. The film of April 11th shows still further improvement in both respects, the lung fields being almost normal. The April film is not strictly comparable because of overexposure, but when studied with an extra bright illuminator the above conclusions were reached.

SUMMARY AND CONCLUSIONS

Serial x-ray film studies were done on patients with bronchial asthma and associated chest pathology who were treated with intramuscular trypsin. Three cases are offered for study and comparison along with the readings of the consulting radiologist and of a reviewing radiologist. The difficulties of comparative radiology are outlined. The progress observed in certain types of chest disease, wherein the inspissation of tenacious mucus is a cardinal symptom, is reported with the use of intramuscular trypsin. In consideration of the subjective and objective findings, further studies are being carried on with particular reference to emphysema and bronchiectasis.

Acknowledgment: The author wishes to express his appreciation to Dr. M. Reingold, who was the Consulting Radiologist, and Dr. W. E. Chamberlain, who was the Reviewing Radiologist. This study was made possible through the kind cooperation of Dr. Gustav Martin and Mr. William Swain of the Clinical Research Department, National Drug Company.

RESUMEN Y CONCLUSIONES

Se hicieron series de radiografías de tórax de los enfermos con asma bronquial y patología asociada que fueron tratados con tripsina intramuscular. Tres casos se ofrecieron para estudio y comparación junto con las lecturas del radiólogo consultante y un radiólogo revisor. Se señalan las dificultades de la radiología comparativa. Los progresos notados en ciertos tipos de enfermedades del pecho en los que domina la obstrucción por mucosidad sólida como síntoma cardinal, se relatan después del uso de la tripsina intramuscular.

Considerando los hallazgos objetivos y subjetivos se hacen más estudios especialmente con relación al enfisema y a la bronquiectasia.

RESUME

Des séries de radiographies ont été pratiquées chez des malades atteints d'asthme bronchique et d'affection thoracique associée, qui étaient traités par la trypsine intramusculaire. Trois cas furent choisis pour être étudiés et comparés avec les interprétations du radiologiste consultant et d'un radiologiste supervisant les cas. Les difficultés de la radiologie comparative ont été définies. L'auteur signale les progrès observés dans certains types d'affection thoracique, où l'épaississement du mucus est un symptôme majeur, après utilisation thérapeutique de trypsine par voie intramusculaire. En considération des données subjectives et objectives, des études ultérieures sont entreprises particulièrement en ce qui concerne l'emphysème et la bronchiectasie.

ZUSAMMENFASSUNG UND SCHLUSSFOLGERUNG

Es wurden Röntgenreihenuntersuchungen vorgenommen bei Kranken mit Bronchialasthma in Verbindung mit krankhaften Thoraxbefunden, die i.m. mit Trypsin behandelt wurden. 3 Fälle werden vorgestellt zur Auswertung und zum Vergleich zusammen mit den Befunden des beratenden Röntgenologen und eines zugezogenen Röntgenologen. Die Schwierigkeiten der vergleichenden Radiologie werden hervorgehoben. Die bei gewissen Arten von Thorax-Erkankungen, bei denen die Eindickung eines zähen Schleimes ein Kardianlsymptom ist, beobachteten Besserungen durch Gebrauch von Trypsin i.m. werden vorgetragen. In Erwägung der subjektiven und objektiven Befunde werden weitere Untersuchungen ausgeführt unter besonderem Bezug auf Emphysem und Bronchiektasie.

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Incidence of Relapses Among Patients Treated with Antibiotics and Chemotherapy

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The purpose of this report is to present the results of our observations on private patients and those treated in a dispensary under our direction in a southern province of Spain.

Material and Methods

Two groups of 1,000 patients each are included in this evaluation. The first thousand belong to the dispensary and include people from the lower social and economical levels. Those having better means, able to pay their medical care, are included in the second thousand.

Half of the patients in the dispensary were treated during the early antituberculosis drug era, and the other 50 per cent were treated after these drugs were readily available and adequate dosage was given.

Also the group from private practice was divided in the same proportion.

The patients belonging to the early era were all treated according to our directions. The second group coming to us, as a rule, had already received treatment by their doctors or even self prescribed.

We have separated the group of children from that of adults and tried to show when treatment was insufficient, poorly indicated, early abandoned, or started too soon.

Results:

RELAPSES INCLUDING ALL 2,000 PATIENTS: ADULTS 172

	Number of Cases	Per Cent
Of old lesions	128	6.40
New foci	44	2.20
No provocative cause was found	171	8.55
New contagion	1	0.05
Adequate treatment	72	3.60
Inadequate treatment	100	5.00

This among the 2,000 cases, 172 (8.60 per cent) relapses were found. Reactivation of old lesions was found in 128 (6.4 per cent) of cases and new foci in 44 (2.20 per cent) of cases.

This, among 2,000 histories we found 74 (3.60 per cent) relapses.

Of which 58 (2.9 per cent) occurred in the same location of the earlier disease and 16 (0.8 per cent) were in new locations.

In six cases the cause of relapses has been found (contagion, reactivity

Read at the IV Congress of Chest Diseases—Cologne, Germany—Aug. 1956.

CHILDREN: 74 (3.70 per cent) Cases		
		Per Cent
Of old lesions	58	2.90
New lesions	16	0.80
No provocative cause found	68	3.40
The cause found in	6	0.30
Adequate treatment	48	2.40
Inadequate treatment	26	1.30
Location of reinfection:		
Pleura	4	0.20
Lymph nodes	35	1.75
Parenchyma	35	1.75

provoked by treatment, respiratory acute conditions). No cause for the rest or 68 cases could be found.

In 48 of the 74 children treatment was completed but this was impossible in 26.

The total of relapses was 246 (12.30 per cent) including children and adults.

In the whole group the new lesion was a reactivation of the old one in 186 (9.30 per cent) cases.

New foci appeared in 60 (3 per cent).

Causes probable responsible were found in seven (0.35 per cent) cases.

Cause unknown: 239 (11.95 per cent).

TOTAL IN CHILDREN AND ADULTS: 246 Cases (12.30) Per Cent		
Of old lesions	186	9.30
New lesions	60	3.00
With known cause	7	0.35
Cause unknown	239	11.95
Adequate treatment	120	6.00
Inadequate treatment	126	6.30

Discussion

The total of antituberculosis drugs used in every case could not be determined with precision. However we considered as TREATMENT COMPLETED those continued during five or six months as a minimum, with INAH and PAS, simultaneously, or alternatively, with at least 50 grms. of SM.

Nine of the 246 patients have had two relapses as follows:

Pleuritis:	2
Adenopathy:	3
Nodular productive forms (postindurative reaction):	4

However these double relapses have been considered once in each instance in the statistics.

Interruption of the treatment early after the apparent cure was obtained, might be responsible for the lack of chances to develop natural immunity, with the resulting susceptibility toward the reinfection.

Too often the normal sedimentation rate, and false negative sputum may lead to consider erroneously healed some cases still carriers of active lesions.

Our results are strikingly similar to those obtained by Bruno Besta in Italy and Prof. Langer of Vienna.

SUMMARY

Two groups of 1,000 patients each are presented. One group is from a dispensary and the other from private practice.

Each 1,000 is subdivided into the first 500 in each group treated in the early antituberculosis drug era and the second 500 in each group after drugs became readily available.

Among the 2,000 reactivations occurred in 186 and new lesions evolved in 60, making a total of 246.

Treatment was considered adequate when antituberculosis drugs had been administered at least six months.

RESUMEN

Se presentan las observaciones de recaídas entre el tratamiento por medio de antibióticos y quimioterapia en 2,000 personas.

Se presentan las estadísticas de las recaídas de los casos sujetos a quimio-antibioterapia de la tuberculosis.

Se observaron dos grupos iguales, de 1,000 personas cada uno correspondiendo el primero a la primera época de aplicación de antibióticos y quimioterapia, cuando los enfermos no recibieron suficientes dosis o no fueron tratados por tiempo suficientemente largo y otro millar es el de casos que han sido tratados más tarde, siguiendo planes más definidos, gracias a la mejor posibilidad de obtener las drogas y a una mejor orientación terapéutica.

Las recaídas en el total de 2,000 enfermos, adultos fueron: 172 (8.60%) que se dividen en dos grupos: Brotes sobre lesiones antiguas: 128 (6.40 por ciento) y brotes sobre focos nuevos: 44 (2.20 por ciento).

Se encontró la causa provocadora en 171 (8.55 por ciento) y se consideraron debidos a contagio nuevo: 1 (0.05 por ciento).

El tratamiento fué adecuado en 72 de los que sufrieron recaídas (2.60 por ciento) y no lo fué en 100 casos (5 por ciento). Entre los niños se encontraron 74 casos (3.70 por ciento). Sobre lesiones antiguas: 58 (2.90 por ciento). Sobre lesiones nuevas: 16 (0.80 por ciento).

No se encontró la causa provocadora en 68 (3.40 por ciento), y se encontró en 6 (0.30 por ciento).

Tuvieron tratamiento adecuado 48 (2.40 por ciento) y no lo tuvieron 26 (1.30 por ciento).

La reinftcción se localizó en:

Pleura: 4 (0.20 por ciento), Ganglios: 35 (1.75 por ciento) y Parénquima: 35 (1.75 por ciento).

Entre los niños, las recaídas fueron de 3.70 por ciento.

El total de recaídas fué de 246 o sea el 12.30 por ciento incluyendo niños y adultos. En general la lesión nueva se desarrolló sobre la antigua en 186 casos. (9.30 por ciento) y fué en focos nuevos en 60 (3 por ciento).

No pudo determinarse en todos los casos el total de antibióticos usados. Sin embargo, consideramos como *tratamiento completo* el que por lo menos se hizo durante 5 a 6 meses con INAH y PAS simultáneamente o alternativamente asociados a SM por lo menos en cantidad de 50 grms.

Algunos enfermos tuvieron dos recaídas: Doble reactivación entre 246: 9 casos. Tales fueron: Pleuritis: 2; Adenopatías: 3 y Formas nodulares productivas (reacción postindurativa): 4.

Estas recaídas en la estadística sólo se han considerado una vez.

Contrariamente a lo esperado, las recaídas fueron menos frecuentes entre niños que entre adultos lo que probablemente se debe a una mejor indicación en los niños. Esto fué discutido con J. Oriol y estuvimos de acuerdo en que la quimioterapia tiene una acción más decisiva en la tuberculosis primaria: actúan en efecto sobre enfermedad temprana entre los niños, en tanto que en los adultos se trata de formas secundarias o terciarias. En el caso de los niños, la quimioantibioterapia puede hacer desvanecerse el substracto patrocrómico, en tanto que en los adultos el mismo substracto precedió a la reactivación y como es lógico permanecerá después de la terapia.

La interrupción pronta después de la cura aparente puede serla causa de la falta de posibilidades de desarrollar inmunidad natural con la resultante susceptibilidad a la reinfección o a la recidiva.

Muy a menudo la sedimentación normal y la falsa negatividad de los esputos puede conducir a considerar curadas erróneamente algunos casos que aún son portadores de enfermedad activa.

Nuestros resultados son notablemente semejantes a los obtenidos por Bruno Besta en Italia y por el Prof. Langer en Vienna.

RESUME

L'auteur présente deux groupes comportant chacun 1.000 malades. Un groupe provient d'un dispensaire et l'autre de la clientèle privée.

Chaque groupe de 1.000 est subdivisé en un groupe de 500 premiers malades—traités pendant la première phase de l'utilisation des produits antibacillaires—et le second groupe de 500 malades, traités après que les médications fussent devenues facilement disponibles.

Sur ces 2.000 malades, des rechutes survinrent chez 186 et de nouvelles lésions évoluèrent chez 60, donnant un total de 246 atteintes.

Le traitement était considéré comme convenable lorsque les médications antituberculeuses avaient été administrées au moins pendant six mois.

ZUSAMMENFASSUNG

Es wird über 2 Gruppen von je 1000 Patienten berichtet. Die eine Gruppe kommt aus einer Fürsorgestelle und die andere aus einer freien Praxis.

Jeweils 1000 werden in jeder Gruppe unterteilt in die ersten 500, die in der frühen antituberkulösen Arzneimittel-Ära behandelt wurden, und die zweiten 500 in jeder Gruppe, die behandelt wurden, nachdem diese Arzneimittel leicht zur Verfügung standen.

Unter dem 2000 Kranken kamen 186 Reaktivierungen vor, und neue Herde entwickelten sich in 60 Fällen, d.h. insgesamt 246.

Die Behandlung wurde als entsprechend bezeichnet, sofern antituberkulöse Arzneimittel wenigstens 6 Monate lang gegeben worden waren.

SECTION ON CARDIOVASCULAR DISEASES

Group A Beta Hemolytic Streptococci and Rheumatic Fever in Miami, Florida: I. Bacteriologic Observations from October 1954 through May 1955

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The etiologic relationship reported to exist between group A beta hemolytic streptococci and rheumatic fever may be influenced profoundly by factors other than the mere presence of the indicated organisms.

Bacteriologic studies[1] from February through May 1953 on monthly cultures of throat swabbings taken from 343 children attending the first grade of three Miami public schools, revealed that 16.3 per cent of the children had a group A streptococcus in their throats at least once (in four months). Similar study[2] of 417 children in the first two grades in the same three schools, whose throats were swabbed monthly from October 1953 through May 1954, showed that 35.9 per cent of the children harbored group A organisms at least once (in eight months).

Antistreptolysin O (ASLO) determinations[2] were carried out on sera from as many of the children in the 1953-54 series as would permit blood-drawing. Samples were taken every two months. Those children who harbored typable or non-typable strains of group A beta hemolytic streptococci, as well as those from whose throats groups C and G organisms were isolated (streptolysin-O producing[3]), had on the average, higher titers than those from whom no beta streptococci, or only group B (non-streptolysin-O producing[3]) organisms were recovered.

The completed investigations pointed out the need for further studies. First, blood samples collected at the arbitrarily set interval of once every two months had the disadvantage of not reflecting adequately anistreptolysin-O response to streptococcal infection; a better correlated time relationship between throat cultures and serum ASLO titers appeared necessary. Second, in the survey period, 1953-54, the children who were absent from school during the times scheduled for taking swabs and bloods were missed completely for the entire month on those occasions. The school nursing staff attempted to determine the cause of absence in each instance. However, the data were incomplete, and more accurate information was

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Supported in part by funds from the Florida State Board of Health and grant H-1738, Public Health Service.

TABLE I
NUMBER OF CHILDREN FROM WHOSE THROATS GROUP A STREPTOCOCCI WERE RECOVERED LISTED BY AGE, SEX AND SCHOOL. BASELINE STUDY, OCT. 1954-MAY 1955

Sex	Age	6-7				7-8				8-9				Total 6-9			
	School	K*	C*	D*	T†	K	C	D	T	K	C	D	T	K	C	D	T
M	Number of Cultures taken	228	174	179	581	107	111	101	319	164	65	82	311	499	350	362	1211
	Number of Children	33	23	24	80	14	15	13	42	22	9	11	42	69	47	48	164
	Number of Children with ABHS	14	8	13	35	6	5	5	16	5	2	4	11	25	15	22	62
	Per Cent of Children with ABHS	42.4	34.8	54.2	43.8	42.9	33.3	38.5	38.1	22.7	22.2	36.4	26.2	36.2	31.9	45.8	38.3
F	Number of Cultures taken	186	136	250	572	112	67	132	311	128	90	125	343	426	293	507	1226
	Number of Children	29	20	34	83	15	9	17	41	16	12	17	45	60	41	68	169
	Number of Children with ABHS	12	6	17	35	7	4	7	18	6	6	10	22	25	16	34	75
	Per Cent of Children with ABHS	41.4	30.0	50.0	42.2	46.7	44.4	41.2	43.9	37.5	50.0	58.8	48.9	41.8	39.7	50.0	44.4
M + F	Number of Cultures taken	414	310	429	1153	219	178	233	630	292	155	207	654	925	643	869	2437
	Number of Children	62	43	58	163	29	24	30	83	38	21	28	87	129	88	116	333
	Number of Children with ABHS	26	14	30	70	13	9	12	34	11	8	14	33	50	31	56	137
	Per Cent of Children with ABHS	41.9	32.6	51.7	42.9	44.8	37.5	40.0	41.0	28.9	38.1	50.0	37.9	38.8	35.2	48.3	41.1

*K = High income white
C = Low income white
D = Mixed income negro
†T = Total

desirable. A third problem the previous studies raised was the extent to which the data obtained in the three schools could be extended to the 35,000 children, ages six to nine, attending public schools throughout Dade County, Florida.

The present investigation was designed: (1) To establish more firmly the previous information by adding data for another school year; (2) to correlate more closely the recovery of beta hemolytic streptococci from the throats of children, with the effects of the presence or absence of these organisms on the ASLO responses; (3) to obtain more accurate results by including the findings of throat and blood studies performed on absentees; and (4) to determine whether the percentages of streptococci recovered in the three schools of the previous studies were approximately the same when applied to all the children of the same age group, attending school throughout Dade County.

Material and Method:

All throat cultures were handled as in the 1953-1954 period[2], except where minute colonies of beta hemolytic streptococci were encountered. Such colonies were emulsified on the initial plate with a tiny loopful of neopeptone infusion broth (Difco) (NEO) and the droplet was used for restreaking the subsequent NEO plate; this procedure helped to insure against loss of tiny colonies. All subcultures from such colonies were incubated under CO_2 in a candle jar, since we had confirmed the observations[4,5] that growth of minute streptococci is enhanced by incubation under increased CO_2. Media were the same as in the previous studies; the isolation

FIGURE 1: Outline map, State of Florida, indicating location of Dade County.

TABLE II

FINDINGS OF BETA HEMOLYTIC STREPTOCOCCI IN 1200 CHILDREN IN COUNTY-WIDE STUDY, OCT. 1954-MAY 1955

No.	Color W	Color N	Date	No. Cult.	Total BHS	Non Gp. A B	Non Gp. A C	Non Gp. A F	Non Gp. A G	Group A Ao	A_1	A_2	A_3	A_4	A_5	A_6	A_7	A_{12}	A_{25}	A_{28}	A_{30}	A_{31}	No.	Per Cent
(1)*	x		10/25/54	25	2					2													2	8.0
(2)	x		10/25/54	25	2	1												1					1	4.0
(3)	x		10/25/54	25	1					1													1	4.0
(4)	x		10/26/54	24	3	1			1													1	1	4.0
(5)	x		10/26/54	26	4				2	1								1					2	8.0
(6)		x	10/26/54	25	4		2		1	1													1	4.0
T. Oct.	x			125	12	2	0	0	3	4								2				1	7	5.6
		x		25	4		2		1	1													1	4.0
	x	x		150	16	2	2	0	4	5								2				1	8	5.3
(7)	x		11/22/54	25	8		1		1	6													6	24.0
(8)	x		11/22/54	25	5				1	4													4	16.0
(9)	x		11/22/54	25	5		1			3								1					4	16.0
(10)	x		11/23/54	25	11	2	1		2	5				1									6	24.0
(11)	x		11/23/54	25	4					3				1									4	16.0
(12)	x		11/23/54	25	4				3					1									1	4.0
T. Nov.	x			150	37	2	3	0	7	21				3				1					25	16.7
(13)	x		1/24/55	25	3		1			2													2	8.0
(14)		x	1/24/55	25	7		2			4				1									5	20.0
(15)	x		1/24/55	25	6	1		1	1	3													3	12.0
(16)	x		1/25/55	24	3		1		1	1													1	4.0
(17)	x		1/25/55	26	7				1	4								2					6	24.0
(18)	x		1/25/55	25	4			1		2								1					3	12.0
T. Jan.	x			125	23	1	2	2	3	12								3					15	12.0
		x		25	7		2			4				1									5	20.0
	x	x		150	30	1	4	2	3	16				1				3					20	13.3

(19)	x		2/21/55	25	2					1			1								2	8.0
(20)	x		2/21/55	25	5		1			3							1				4	16.0
(21)	x		2/21/55	25	6	2			2	2											2	8.0
(22)	x		2/22/55	23	7			1	1	2					1		1		1		5	20.0
(23)	x		2/22/55	27	10		1	1		6	1			1							8	32.0
(24)	x		2/22/55	25	8		1	1	1	3	1						1				5	20.0
T. Feb.	x			150	38	2	3	3	4	17	2		1	1	1		3		1		26	17.3
(25)	x		3/21/55	25	4				1	3											3	12.0
(26)	x		3/21/55	25	8		1	1		3		1					1	1			6	24.0
(27)	x		3/21/55	25	8		1	1		2			1		1		2				6	24.0
(28)	x		3/22/55	25	7			1		4	1		1								6	24.0
(29)	x		3/22/55	25	3		1			1			1								2	8.0
(30)	x		3/22/55	25	9	1	1				6						1				7	28.0
T. Mar.	x			150	39	1	4	3	1	13	7	1	3		1		4	1			30	20.0
(31)	x		3/28/55	25	2					1										1	2	8.0
(32)	x		3/28/55	25	6		1			2	2					1					5	20.0
(33)		x	3/28/55	25	9	1	2	1	3	1						1					2	8.0
(34)	x		3/29/55	25	6			1	1	4											4	16.0
(35)	x		3/29/55	25	8	3				3			1				1				5	20.0
(36)	x		3/29/55	25	5				2	2		1									3	12.0
T. Apr.	x			125	27	3	1	1	3	12	2	1	1			1	1			1	19	15.2
		x		25	9	1	2	1	3	1						1					2	8.0
	x	x		150	36	4	3	2	6	13	2	1	1			2	1			1	21	14.0

TABLE II (Continued)

FINDINGS OF BETA HEMOLYTIS STREPTOCOCCI IN 1200 CHILDREN IN COUNTY-WIDE STUDY, OCT. 1954-MAY 1955

No.	Color W	Color N	Date	No. Cult.	Total BHS	Non Gp. A B	Non Gp. A C	Non Gp. A F	Non Gp. A G	Group A Ao	A_1	A_2	A_3	A_4	A_5	A_6	A_7	A_{12}	A_{28}	A_{32}	A_{34}	A_{41}	No.	Per Cent
(37)	x		5/23/55	25	3	1		1		1													1	4.0
(38)	x		5/23/55	25	3	1			1	1													1	4.0
(39)	x		5/23/55	25	6		1		1	4													4	16.0
(40)	x		5/24/55	25	3				2	1													1	4.0
(41)	x		5/24/55	25	6	1			1	3						1							4	16.0
(42)		x	5/24/55	25	13		4		6	2	1												3	12.0
T. May	x			125	21	3	1	1	5	10						1							11	8.8
		x		25	13		4		6	2	1												3	12.0
	x	x		150	34	3	5	1	11	12	1					1							14	9.3
(43)	x		5/30/55	25	5				1	1	2		1										4	16.0
(44)		x	5/30/55	19	5		2		1	2													2	10.5
(45)	x		5/30/55	31	12			1	1	7	3												10	32.2
(46)		x	5/31/55	23	5		3	1		1													1	4.3
(47)	x		5/31/55	27	10	1	2		2	1			1					3					5	18.5
(48)		x	6/ 3/55	25	9		3		1	5													5	20.0
T. June	x			83	27	1	2	1	4	9	5		2					3					19	22.9
		x		67	19		8	1	2	8													8	11.9
	x	x		150	46	1	10	2	6	17	5		2					3					27	18.0
	x			1033	224	15	16	11	30	98	16	2	10	1	3	1	17	1	1	1	1		152	14.7
Grand		x		167	52	1	18	2	12	16	1	0	1	0	0	1	0	0	0	0	0		19	11.4
Totals	x	x		1200	276	16	34	13	42	114	17	2	11	1	3	2	17	1	1	1	1		171	14.25

*Numbers correspond to county map (figure 2).

and identification were as before. Grouping and typing again were performed at the Streptococcus Laboratory, Communicable Disease Center, Public Health Service, Chamblee, Ga., under the supervision of Dr. Elaine L. Updyke.

Baseline Study:

Throats of children attending three public schools of Dade County, Florida, were swabbed as in our previous studies[1,2]. A total of 2437 pairs of swabs were taken from the throats of 333 children six to nine years of age during the eight-month period, October 1954 through May 1955. Each child's throat was swabbed an average of 7.3 times. The three schools were the same ones selected in the two previous years of study, representing a low income white (C), a high income white (K) and a mixed income Negro (D) population. Children in the second and third school years had participated in one or two years of the preceding investigation.

Maximum school enrollment in Dade County, Florida, for the first, second and third grades totalled 35,350 during the 1954-1955 school year. Thus

FIGURE 2: Outline map of Dade County, Florida. Numbers refer to order in which schools were visited (cf. table II).

TABLE III

CHILDREN PARTICIPATING IN 2 YEARS OF STREPTOCOCCAL STUDY (OCT. 1953-MAY 1955): POSITIVE FOR BETA HEMOLYTIC STREPTOCOCCI IN EACH OF 2 YEARS

		1953			1954									1955					
		Oct.	Nov.	Dec.	Jan.	Feb.	Mar.	Apr.	May	Oct.	Nov.	Dec.	Jan.	Feb.	Mar.	Apr.	May
K	2070		Ao		Ao												Ao
	2072	Ao	Ao		Ao	Ao			Ao	Ao	Ao	Ao	Ao	Ao	Ao		Ao
	2080	C				Ao			Ao	Ao		Ao					Ao
	2082							C		C	C	C					
	2131	A_{12}													A_6	A_6	A_6
	2132								A_1			Ao					
C	2364		Ao	Ao								Ao	Ao	Ao	Ao		
	2367	G	A_{25}	G	G	G	G										F
	2374	Ao						B					F	F	Ao	Ao	Ao
D	2695								Ao	Ao + B				Ao			
	2678								C	C							
	2696		Ao		Ao				Ao	C			C	C			
	2667	Ao				Ao				G				G	G	G	
	2668								G			G					
	2669	G		G						Ao + A_{44}	Ao	Ao	Ao	G + A_{15}		G + A_{20}	
	2673				G											G	
	2679		C							Ao	Ao	Ao				C	
	2684				Ao								Ao			A_{32}	
	2685					Ao				Ao + G	Ao + G		G	G			F + G
	2689	Ao						C	C				Ao + C				
	2691	Ao	Ao + G					C	Ao + C		C					C	C
	2694							G							Ao		

the number of children in this portion of the survey represented 0.94 per cent of the entire group of school children of this age.

Venous blood was drawn from every child at the time the first throat culture was taken, and again when the last swabbing was done. If a beta hemolytic streptococcus was isolated from any child's throat, whether from the first or any subsequent swabbing, throat cultures and blood samplings were repeated two, four and eight weeks later, then bimonthly through May 1955. Five hundred ninety-eight additional paired throat cultures were taken in this section of the study. In a few instances, continued positive throat cultures resulted in the collection of 16 biweekly samples during the eight months. The use of silicone-coated Vacutainers* markedly simplified the blood-drawing, and reduced the percentage of hemolyzed samples obtained. Each blood sample was centrifuged, the serum separated from the cell clot, and the serum deep-frozen until June 1955, when ASLO titer determinations were performed[6], using commercial Difco streptolysin-O.

In contrast to the earlier studies[1,2], every effort was made in the present study to obtain required throat cultures and blood samples from every child, as scheduled, whether or not the child was present in school. This was accomplished in one of two ways. Often, a technician was detailed to go to the homes of children who were absent on regularly scheduled culturing days, within 72 hours of the absence. Occasionally, a parent was reluctant to permit the technician's visit. In such a case, samples were not obtained at that particular time. In most instances of absenteeism, samples were collected at the school when the child returned to class within three days of the absence. No follow-up was attempted on any child absent on days other than those set for study at school.

There were only 286 children left in the study by May 1955, of the 333 who began in October 1954 (a loss of 14.1 per cent). Because of the frequency of blood-drawing, many parents withdrew their children from the study. Other families moved to different school districts. (We do not know if these transfers were related to our study).

County-wide Study:

In addition to the 333 children in the three schools of the baseline study, 1920 additional children six to nine years of age attending grades one, two and three were studied. Forty children in each of 48 additional schools (of the total of 76 elementary schools in Dade County) were canvassed at random for throat swabbing one time only. On two mornings per month, from October 1954 through June 1955, excluding December because of Christmas holidays, three different schools were visited (six schools per month for a total of 48 schools). The first 25 children in each school presenting parentally signed permission slips had their throats swabbed. These children were studied once only. Figure 1 is a geographic sketch of the State of Florida, indicating the location of Dade County. Figure 2 shows the sequence and distribution of schools studied in the county-wide sampling. A total of 1200 pairs of cultures were collected (3.4 per cent of the total county-wide enrollment). No blood samples were taken from these children.

*Kindly supplied by Becton-Dickinson Co., Rutherford, N. J.

TABLE IV

CHILDREN PARTICIPATING IN 3 YEARS OF STREPTOCOCCAL STUDY (FEB. 1953-MAY 1955): POSITIVE FOR BETA HEMOLYTIC STREPTOCOCCI IN 2 OR 3 YEARS

		1953							1954									1955				
		Feb.	Mar.	Apr.	May	Oct.	Nov.	Dec.	Jan.	Feb.	Mar.	Apr.	May	Oct.	Nov.	Dec.	Jan.	Feb.	Mar.	Apr.	May
K	2097			A_{12}			A_{12}			A_{12}											
	2098									Ao						F				F	
	2102			A_{12}										Ao			Ao	Ao		Ao	Ao
	2114									A_1							A_1				
	2122									A_{38}	Ao	Ao	Ao	A_{32}	A_{35}				A_{38}	A_{37}	A_{30}
	2123									A_{12}		A_{12}	A_{12}	Ao	Ao	Ao	Ao	Ao	Ao	Ao	
	2125										Ao							Ao			
	2126											A_4								A_4	
	2139			NG						Ao	A_{44}										
C	2353									G			G	G	G	G		G	F + G		
	2359								Ao		Ao						Ao	Ao			Ao
	2383			A_{12}			G			G + A_{12}				Ao + A_{12}	Ao	A_6					
	2384			A_{12}	C																
	2389			A_{12}					A_{12}			Ao	Ao	Ao	Ao	Ao	Ao		Ao	Ao	
D	2702											Ao	Ao		A_{12}	A_{17}	A_{12}	A_{12}	A_{12}		
	2703												Ao	C			C			C	C
	2706				Ao						B			Ao						A_{12}	F
	2709				Ao									G	Ao	Ao	Ao + G			Ao + G	
	2710										G			G					G + C	C	C
	2711				Ao													Ao			
	2712												Ao		C	Ao + C					
	2713												C	C	C		C	C	C	C	C
	2716				B			C	C	C			Ao + C	Ao	Ao		G	Ao	A_{43}		
	2718							Ao + A_{12}									Ao	Ao	Ao	Ao	
	2720					C				C			Ao	C				C	C	C	C
	2721		Ao			C	G			C	C	C		C	C	C	C	C	C	C	C + A_{26}
	2723			A_{12}		G					G					Ao	Ao		C	C	C

Results

Baseline Study:

Beta hemolytic streptococci were removed at least once during the eight-month period, October 1954 through May 1955 from the throats of each of 198 children of the 333 students intensively studied in the three schools. The average number of children cultured per month was 304.6. Streptococci were recovered from approximately the same percentage of children in each of the two white schools (50.4 and 54.5 per cent) but in much higher numbers (73.3 per cent) from the Negro school. For each of seven of the eight months of the study, the isolation rate of all β streptococci was higher in negro children. The results obtained in the isolation of β hemolytic streptococci other than group A, are the subject of a separate communication. Total positive cultures were recovered from 24.7 per cent of the 2437 cultures studied; the monthly findings were: October 1954, 21.3 per cent; November, 21.0 per cent; December, 19.3 per cent; January 1955, 24.3 per cent; February, 27.6 per cent; March, 27.9 per cent; April, 30.0 per cent; and May, 27.6 per cent.

Of the 333 children participating in this portion of the present investigation, 137 children (41.1 per cent) bore these organisms in their throats at

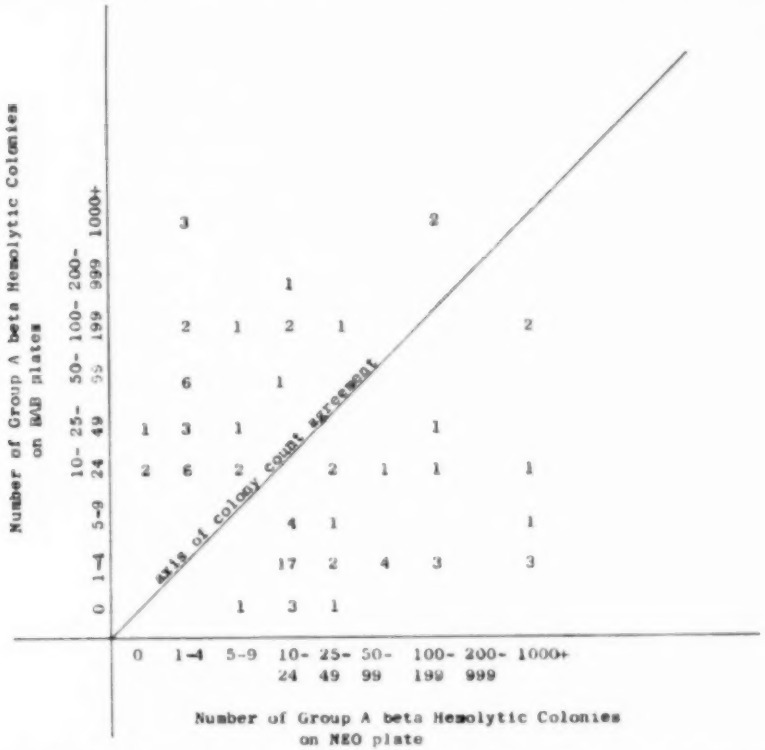

FIGURE 3: Comparison of colony counts on BAB vs. NEO of 82 pairs of plates (of a total of 345) from individual children harboring ABHS, in which a discrepancy in colony counts was noted. Baseline study, Oct. 1954-May 1955. *Example*: "17" in the figures indicates that in each of 17 paired cultures, 10-24 ABHS colonies were recovered on NEO; the BAB plates yielded only 1-4 ABHS colonies.

least once. In 20 instances, additional group A organisms from the throats of these 137 children were identified by change in Lancefield type. Since the average number of children participating monthly was 304.6 the corrected *average* rate of recovery of group A streptococci rises from 41.1 per cent (137/333) to 44.7 per cent (137/304.6).

Of the 2437 routine *monthly* cultures (not including the midmonthly swabbings done on those children who harbored streptococci at the time of the monthly culturing), 1568 (64.3 per cent) were from white children; 869 (35.7 per cent) were from negro children. Midmonthly throat swabbings were performed 598 times, which, when added to the 2437 pairs of monthly swabbings for the eight-month period, brought the total number of baseline cultures to 3035. The total number of group A isolates at monthly culturing only, was 153, of which 58.2 per cent were from white children; 41.8 per cent from negro. The 153 group A streptococcal isolates were from 136 children.

Table 1 presents the number and per cent of children harboring group A β hemolytic streptococci, listed according to age, sex and school. The percentage of children harboring these organisms dropped slightly as the age of the children increased (42.9 per cent for children six to seven years; 41.0 per cent for seven to eight; 37.9 per cent for eight to nine). Girls showed a higher rate than boys (44.4 per cent as against 38.3 per cent). The two white schools had approximately similar rates (38.8 per cent and 35.2 per cent), while the negro school rate was considerably higher (48.3 per cent). Despite the higher percentage of negro children to be found to be bearing group A streptococci in their throats, the rate of positive cultures per total number of cultures taken in the school was approximately the same in the three schools studied; 14.3 per cent for the negro school, 15.0 and 12.8 per cent for the two white schools. The overall monthly recovery rate of group A β hemolytic streptococci was: October 1954, 10.2 per cent; November, 13.3 per cent; December, 12.0 per cent; January 1955, 12.5 per cent; February, 16.8 per cent; March, 16.9 per cent; April 15.3 per cent; May, 17.1 per cent.

Ten different typable strains of group A β hemolytic streptococci recovered from the throats of children in the baseline study were represented (types 1, 4, 6, 11, 12, 13, 33, 39, 43 and 44). Type 6 strains were most common (54 strains) and type 4 next most common (37 strains). Type 6 strains were isolated in large numbers in March, April and May, 1955 although a few strains had been recovered in December 1954, January and February 1955. All other Lancefield types were recovered throughout the study period in scattered fashion without clustering in any one month.

County-wide Study:

The findings of all β hemolytic streptococci, including group A organisms, typable and nontypable in the 1200 children comprising the county-wide study are detailed in table 2. Swabbings taken from white children constituted 1033 (86.1 per cent) while those from negroes were 167 (13.9 per cent). Positive cultures were obtained from 224 (81.2 per cent) of the whites and from 52 (18.8 per cent) of the negro children, but group A organisms were found in only 19 (11.1 per cent) of the negro children, and

152 (88.9 per cent) of the white pupils. Thus, in this portion of the study, β hemolytic streptococci were recovered more commonly from negroes than whites, but group A streptococci were more frequent in white children.

Monthly recovery rates of group A β hemolytic streptococci were tabulated for both the baseline and the county-wide studies. The baseline rate varied from 10.2 per cent per month to 17.1 per cent; the county-wide limits were 5.3 and 20.0 per cent. However, the number of cultures taken monthly in the county-wide study was half the number taken in the baseline study. The average monthly rates in the two groups, were almost identical, 14.16 and 14.25 per cent respectively. The ratio of white to negro children studied was approximately the same in baseline and county-wide programs.

The relationship of sex and age to the rates of recovery of group A β hemolytic streptococci were tabulated for the 750 children (in 30 of the 48 schools studied), for whom data as to age were collected. The drop in percentage seen in the baseline study, of group A streptococci recovered with increasing age of the children was observed also in the county-wide study (ages six to seven, 17.8 per cent; seven to eight, 17.5 per cent; eight to nine, 11.7 per cent). Again as in the baseline study, the ratio of percentages of group A isolates recovered from boys as compared with girls, showed that six to seven year old boys harbored more of these organisms than did girls of the same age (19.3 per cent for boys; 16.5 per cent for girls); in the seven to eight year age group, approximately the same percentage of boys (17.8 per cent) and girls (17.2 per cent) carried these organisms; the percentages were completely reversed in the eight to nine year old children (9.1 per cent for boys; 13.8 per cent for girls).

A_6 Epidemic:

During March, 1955, the children attending one school (K) were found to yield large numbers of group A, type 6 streptococci. Upon close scrutiny of the distribution of these organisms, they appeared to be confined largely to two classes in the first grade. Throat cultures were taken from most of the children attending these two classes. Of 24 children from whom throat cultures were taken in one class, we isolated group A beta hemolytic streptococci from 13; 11 strains of streptococci were type 6 and 2 were nontypable group A organisms. Of 27 cultures taken in the other class, eight were type 6 streptococci and two streptococcal cultures were non-group A. In the first class, on the day these studies were carried out, three children were not sampled because of absence and five others refused to have their throats swabbed. In the second class, seven children were absent. Causes of absence were determined in five of the 10 instances: two had mumps, two had chicken pox, and one, tonsillitis. At that time, chicken pox and mumps were common throughout the schools of Dade County. Thirteen of the 32 children attending the first class and 18 of the 34 in the second class gave histories of respiratory illness within one month prior to the date of the special study. On the culture date, the teacher of the first class had a throat swab negative for beta hemolytic streptococci; however, the teacher of the second class had a severe sore throat, from which group A, type 6 streptococci were isolated. Her clinical symptoms later became so marked that she was forced to remain at home for several days. Of the

10 other teachers of first, second and third grade classes, only one harbored type 6, group A streptococcus; she also had severe clinical symptoms necessitating home care. Eight teachers had negative throat cultures; one harbored a group G organism.

Absences:

Review of the attendance record of each child in the first three grades revealed that about 95 per cent of all children were absent from school at least once during this eight-month school year. The monthly records of the three schools in the baseline study showed the average attendance to vary between 93 and 96 per cent per month. Even during the group A, type 6 "outbreak" there was no noticeable alteration in the monthly absentee rate for this school or for the classes involved. The relationship between streptococcal isolation and absence, along with cause of absence, and antistreptolysin-O responses will be detailed in a subsequent section of this series of reports.

Persistence of Streptococci in the Throat:

In the baseline study, throat swabbings were taken monthly from all children, and repeated two weeks later in those children from whose throats these regular monthly cultures were positive for any beta hemolytic streptococcus. Organisms of the same group or type were isolated repeatedly from the same children. In several children the same group and type of streptococcus was recovered repeatedly during the entire eight-month period (16 isolates). Conversely, change in the group of beta hemolytic streptococcus recovered from the same child was a common occurrence. Organisms of two different groups were isolated sometimes from the same throat swabs. Group A streptococcus was recovered occasionally in combination with organisms of other groups. The combination of a typable and a non-typable group A streptococcus was encountered four times. Never did we isolate group A organisms of two different types from the same child at one culture period, despite the fact that colonies of organisms recovered on initial plating which appeared morphologically different on microscopic examination under low power, were isolated separately and each culture sent for grouping and typing. In routine throat culturing, we observed that one to three month intervals occurred sometimes between recovery of group A organisms of the same identifiable types from any one child.

Of the 333 children who participated in the baseline study, 85 had taken part in the previous year's study[2], and 82 others had been available for culturing over a three-year period.[1, 2, 7, 8] Twenty-two of the 85 children studied for two years were positive for β hemolytic streptococci of the same or different groups and types in each of the two years (table 3); 27 of the 82 three-year participants carried β hemolytic streptococci more than one year (table 4). β hemolytic streptococci were recovered from the throats of four children (C2383, C2389, D2721, D2723) in each of the three years of the investigation, while strains of the same type (group A, type 12) were isolated in each of the three years from the throat of only one child (C2383). This child harbored type 12 organisms in his throat for 17 months.

Technique of Throat Culturing in Duplicate:

In the first complete school year study (Oct. 1953-1954)[2], 38 per cent of all the cultures of group A β hemolytic streptococci recovered were isolated on each of two media, blood agar base (Difco) enriched with 4 per cent defibrinated sheep's blood (BAB), and neopeptone infusion agar (Difco), similarly enriched with sheep's blood (NEO); 27 per cent were isolated on BAB alone and 35 per cent on NEO alone. The corresponding findings for the current year (Oct. 1954-May 1955) were, 60 per cent isolated on both media, 21 per cent on BAB alone, and 19 per cent on NEO alone. Thus, from 1/5 to 1/3 of all positive cultures of group A streptococci would have been lost if a single plate had been used instead of the duplicate technique we employed, regardless of which media had been used alone. The effect on the streptococcal recovery rate of a third and fourth plate for initial culturing is under present investigation.

Colony Counts:

Numbers of colonies of all β hemolytic streptococci observed on initial plates were recorded; 84 pairs of plates of the 345 cultures (24.3 per cent) positive for group A organisms had more than 25 colonies of these organisms on the combined pair of initial plates. More than half (48) of these paired cultures had over a hundred colonies. (Colony counts: 1-4, 140 cultures; 5-9, 64; 10-24, 57; 25-49, 20; 50-99, 16; 100-199, 21; 200-999, 7; 1000+, 20.)

In an attempt to determine the amount of discrepancy between colony counts obtained from each of a pair of throat swabs plated initially on two different media (one swab of each pair on BAB, and the other swab on NEO), arbitrary categories were set up for the evaluation of colony counts of the 345 pairs of cultures, where at least one of each pair of plates was positive for group A β hemolytic streptococci. Figure 3 graphically presents the disposition of the 82 pairs of cultures (23.8 per cent of 345) which yielded substantially different colony counts on the basis presented. Thirty-four pairs of cultures gave higher colony counts of group A β hemolytic streptococci on BAB than on NEO; 48 were higher on NEO than on BAB.

The relationship between the number of colonies on initial plates and antistreptolysin O titers and clinical illness will be reported in future communications.

Discussion

The recovery of group A β hemolytic streptococci from the throats of 44.7 per cent of an average of 304.6 children cultured monthly during an eight-month period, supports our previous observations[1,2] that these organisms are common inhabitants of the fauces of children attending the first three grades of three selected public schools in Miami, Florida. Our county-wide studies indicate that the findings in the baseline study were representative of the entire Dade County school population six to nine years of age.

An "epidemic" of group A type 6 β hemolytic streptococci in one school of the baseline study, although attended by isolation rates of 33 and 50 per cent from the children of the two classes involved, did not appear to

influence the monthly rates of absenteeism in the affected classes, nor in the school concerned. The relationship between absences due to respiratory illnesses and the recovery rate of group A streptococci is the subject of a later communication.[9]

Group A streptococci were observed to be persistent in the throats of many children; the same groups and types of organisms were isolated repeatedly from individual children during many months, up to 17 in one case.

The present study again emphasized the necessity for duplicate swabbing of each child's throat. Loss of about 20 per cent of the total number of positive group A cultures could have occurred if single swabs and single plates had been used throughout this investigation, irrespective of whether BAB or NEO had been employed as the primary medium.

Another factor in streptococcal isolation rates that we considered was the number of β hemolytic streptococcal colonies on initial plates. Colony counts have been stressed as a criterion for the presence or absence of one minor manifestation in the diagnosis of rheumatic fever[10]. However, in considering group A organisms, we observed that marked discrepancies occurred in colony counts from each of the two initial bacteriological plates, prepared from pairs of swabs taken simultaneously from single throats.

Immunologic observations, streptococcal and serological findings among school absentees, bacteriological and immunological findings related to β hemolytic streptococci other than group A organisms, effects of population age on streptococcal isolation rates, and the influence of triple or quadruple swabbing and plating, will be presented in subsequent reports. The relationship of these findings to rheumatic fever and glomerulonephritis will be discussed.

SUMMARY

1. An intensive baseline investigation of group A beta hemolytic streptococci isolated from the throats of children six to nine years of age, was carried out in three public schools in Miami, Florida, by means of monthly throat culturing of 333 children during the school year, October 1954 to May 1955. Concurrently, a county-wide survey was done in 48 additional elementary schools throughout Greater Miami (Dade County); the 1200 children, ages six to nine, in this portion of the study were cultured one time only, at the rate of 150 children per month.

2. Both baseline and county-wide studies confirmed our previous observations (1953, 1953-54) that group A streptococci could be recovered frequently from the throats of children in this most southerly large city.

3. The baseline study revealed that 44.7 per cent of an average of 304.6 children harbored group A organisms at least once during the eight-month school year.

4. Monthly average isolation rates of group A streptococci were 14.16 per cent in the baseline study and 14.25 per cent in the county-wide survey. The similarity in these two rates indicates, we believe, that the baseline study is representative of the county-wide prevalence of group A organisms in the age group, six to nine years.

5. There was a small, but definite, decrease in the streptococcal recovery

rate with advancing age, in six to nine year old children, in both baseline and county-wide investigations.

6. Group A streptococci were isolated from the throats of six to seven year old boys more frequently than girls; the proportion of boys to girls, ages seven to eight, harboring these organisms, was approximately equal; in eight to nine year old children, girls' throats were positive for streptococci much oftener than boys'. This apparent relationship in the 1954-1955 school year, of sex and age to streptococcal recovery rates held for both the baseline and county-wide surveys.

RESUMEN

1. Se llevó a cabo una investigación local del grupo del estafilococo hemolítico A beta aislado de la faringe de niños de seis a nueve años en tres escuelas públicas de Miami, Florida, mediante un cultivo mensual de la garganta de 333 niños durante el año escolar de Octubre de 1954 a Mayo de 1955. Al mismo tiempo se hizo una búsqueca en otras 48 escuelas elementales en los alrededores de Miami (Condado de Dade); en los 1200 niños de seis a nueve años de edad, de este grupo se hizo sólo una vez al cultivo a razón de 150 niños por mes.

2. Tanto el estudio local como el de la región del Condado confirmaron nuestras observaciones previas (1953, 1953-1954) de que el grupo A del estafilococo puede encontrarse frecuentemente en las gargantas de los niños en esta Ciudad tan al Sur.

3. El estudio local reveló que 44.7 por ciento de un término medio de 304.6 niños tenían el germen del grupo A por lo menos una vez durante los ocho meses escolares.

4. El término medio de aislamiento del grupo A cada mes, fué de 14.16 por ciento en el estudio local y 14.24 por ciento en la investigación en el condado. La similaridad de estas dos proporciones indica, creemos, que el estudio local es representativo de la prevalencia en el condado de los organismos del grupo A en la edad de 6 a 9 años.

5. Al avanzar la edad hay un decrecimiento de hallazgos de estreptococo pequeño pero definido entre las edades de seis a nueve años tanto en la investigación local como en la del condado.

6. Se aisló el estreptococo A de las faringes de niños de seis a siete años más frecuentemente que las de niñas; siendo la proporción en ambos grupos ya en las edades de 7 a 9 años aproximadamente igual y de ocho a 9 años la posividad del estreptococo fué mucho más frecuente entre las niñas que entre los niños.

Esta aparente relación en el año escolar de 1954-1955 en sexos y edades para el hallazgo de estreptococos fué la misma para la investigación local que para la del condado.

RESUME

1. Les auteurs ont mené une enquête très complète sur les streptococques hémolytiques du groupe A beta, isolés de la gorge des enfants âgés de 6 à 9 ans appartenant à trois écoles publiques à Miami, Floride. Dans ce but, ils ont utilisé des cultures mensuelles faites sur les prélèvements laryngés de 333 enfants pendant l'année scolaire d'octobre 1954 à mai

1955. En même temps un contrôle portant sur tout le district fut fait dans 48 écoles élémentaires supplémentaires dans le Grand-Miami (district de Dade). Dans cette partie de l'enquête les 1.200 enfants âgés de 6 à 9 ans subirent une fois seulement ces cultures, pour une moyenne de 150 enfants par mois.

2. Les études faites au centre et dans toute l'étendue du district confirmèrent nos observations antérieures (1953, 1953-54) selon lesquelles les streptocoques du groupe A pouvaient être obtenus fréquemment dans la gorge des enfants, dans cette grande cité qui est la plus méridionale.

3. L'étude fondamentale révéla que 44,7% sur une moyenne de 304,6 enfants hébergent des microbes du groupe A au moins une fois pendant leur année scolaire de huit mois.

4. Les taux mensuels moyens d'isolement des streptocoques du groupe A furent de 14,16% dans l'étude faite au centre, et de 14,25% dans de contrôle systématique étendu à tout le district. Les auteurs pensent que la similitude de ces deux moyennes indique que l'étude du centre est représentative de la prévalence des organisms du groupe A dans l'ensemble du district pour le groupe des enfants âgés de 6 à 9 ans.

5. Il y eut une diminution, modeste mais nette du taux des dépistages de streptocoques selon l'âge des enfants, chez les enfants âgés de 6 à 9 ans, à la fois dans l'étude du centre et dans le contrôle de l'ensemble du district.

6. Des streptocoques du groupe A furent isolés de la gorge de garçons âgés de 6 à 7 ans plus fréquemment que chez les filles; la proportion des garçons par rapport aux filles, âgés de sept à huit ans, hébergeant ces germes, fut approximativement égale; chez les enfants âgés de 8 à 9 ans, on trouva des streptocoques dans la gorge des petites filles beaucoup plus souvent que chez les garçons. Ce rapport apparent dans l'année scolaire 1954-55 entre l'âge et la mise en évidence des streptocoques était valable à la fois pour le contrôle du centre et celui du district.

ZUSAMMENFASSUNG

1. Es wurde eine intensive "Basis"—Untersuchung einer Beta haemolytischen Streptococcengruppe A ausgeführt, die aus dem Rachen von 6-9-jährigen Kindern von 3 staatlichen Schulen in Miami (Florida) isoliert wurden mittels monatlicher Kultur vom Rachenabstrich bei 333 Kindern während des Schuljahres von Oktober 1954 bis Mai 1955. Gleichzeitig wurde eine den gesamten Kreis umfassende "Ubersichts"—Untersuchung vorgenommen in 48 weiteren Elementar-Schulen aus Gross-Miami (Kreis Dade); bei den 1200 sechs- bis neunjährigen Kindern dieses Teils der Gesamt—Untersuchungsreihe wurde nur eine einzige Kultur angelegt entsprechend einer Zahl von 150 Kindern pro Monat.

2. Sowohl die "Basis"—wie die "Übersichts"—Untersuchungen des ganzen Kreises bestätigten unsre vorausgegangenen Beobachtungen (1953, 1953-1954), wonach Streptococcen der Gruppe A häufig im Rachen von Kindern dieser am meisten südlich gelegenen Grossstadt angetroffen werden.

3. Die "Basis"—Untersuchung ergab, dass 44,7% eines Durchschnitts von 304.6 Kindern Organismen der Gruppe A mindestens einmal während

des 8-monatigen Schuljahres beherbergten.

4. Die monatlichen Durchschnitte der Isolierung von Streptococcen der Gruppe A lagen bei 14,16% in der "Basis"—Untersuchung und bei 14,25% in der sich über den ganzen Kreis erstreckenden Untersuchung. Die Ähnlichkeit dieser beiden Werte weist nach unserer Überzeugung darauf hin, dass die "Basis"—Untersuchung repräsentativ ist für die im ganzen Kreis bestehenden Häufigkeit der Organismen der Gruppe A in der Altersgruppe von 6 bis 9 Jahren.

5. Es bestand eine geringe, aber deutliche Abnahme in der Entdeckungsziffer für Streptococcen mit zunehmendem Alter zwischen 6- und 9-jährigen Kindern sowohl in der "Basis"—wie der Gesamtkreis—Untersuchung.

6. Streptococcen der Gruppe A wurden häufiger aus dem Rachen von 6-7-jährigen Knaben isoliert als bei Mädchen; das Verhältnis von Knaben zu Mädchen im Alter von 7-8 Jahren, bei denen Erreger vorkamen, war ungefähr gleich; bei 8-9 Jahre alten Kindern waren die Rachenabstriche bei Mädchen häufiger positiv auf Streptococcen als bei Knaben. Diese augenfällige Beziehung für das Schuljahr 1954-1955 hinsichtlich der Streptococcenbefunde nach Alter und Geschlecht bestätigte sich sowohl für die grundlegende wie für die Gesamtkreis—Untersuchungen.

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Pre and Postoperative Care for Patients Undergoing Open Cardiac Surgery

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As considerable and widespread interest in open cardiac surgery has developed, many papers have appeared describing the various techniques and results with use of extracorporeal circulatory systems. However, the important aspects of pre and postoperative care of the open heart patients have received much less attention. This omission is indeed significant for given a group of cardiac patients with a good total body perfusion and a good surgical repair of their cardiac lesions, the difference between a very low operative risk and a higher mortality is often made by the attention given to details of management in the immediate pre and postoperative intervals. Therefore, it may be of value to others to examine suggestions based on experiences gained at the University of Minnesota Hospitals during the past five years in which period more than 700 open cardiac operations were performed.

I. *Preoperative Preparation for Open Cardiac Surgery*:

A. *The Admission of the Patient*:

It is usually advantageous to have the patient enter the hospital at least three days before surgery, and at a time when in the best possible health and free of respiratory tract infection or contagious disease. Indeed this susceptible individual should not be admitted to any ward or station populated by other patients with active respiratory tract disease.

Persons with heart disease, particularly those with an increased pulmonary flow and congested lungs are prone to contract upper respiratory tract infections. Semi-isolation preoperatively prevents undue contact with others harboring organisms from a chronic or residual tracheo-bronchial infection. When the cardiac patient contracts an illness from this source it necessarily leads to postponement of surgery.

Children, particularly, benefit by being allowed several days or more before surgery to adjust to their changed surroundings and to reacquire appetites which are sometimes lost during this transition to hospital routine.

B. *The Preparation of the Operative Field*:

Careful preparation of the skin in the preoperative period helps diminish the incidence and severity of wound infections. This is especially impor-

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Supported by Research Grants From:
1. Graduate School, University of Minnesota.
2. Minnesota Heart Association.
3. American Heart Association.
4. Life Insurance Medical Research Fund.
5. National Heart Institute, Grant No. H-830.

tant in those cases where thoracotomy with transection of the sternum is planned, for the sternal wound lies superficially, being covered only by periosteum, subcutaneous tissue, and skin. A wound infection in this area can spread to involve the sternum and the mediastinum resulting in a prolonged morbidity. We prefer to cleanse thoroughly the skin of the anterior chest and abdominal wall, both axillae, groins and back, by scrubbing it with Phisohex* twice a day for several days immediately prior to operation. A thin layer of this material remains on the skin surface after each scrub. This type of preparation is likewise repeated in the operating room just prior to the application of an antiseptic used to demarcate the operative field.

C. *The Preoperative Use of Antibiotics*:

The preoperative use of antibiotics may be of value in preventing postoperative respiratory complications. We recommend the administration of penicillin for two days prior to surgery, provided no sensitivity exists to this drug. Otherwise erythromycin or chloramphenicol are used. Initially, an oral preparation of penicillin is used but for the 24 hours immediately preceding surgery a parenteral preparation is usually administered.

D. *Diet and Vitamins Preoperatively*:

When no contraindication, such as cardiac failure, is present a general diet supplemented with vitamins C and K** is prescribed. On the morning before the operation, the patient is given a mild laxative, such as milk of magnesia, and a regular diet is allowed until twelve hours before surgery. All intake by mouth is then discontinued, except in infants and children. For them we have provided strained fruit juices supplemented with glucose up to three hours before surgery. This supplies calories as carbohydrate, prevents starvation ketosis, and hence minimizes the danger of postoperative acidosis.

E. *Preoperative Hematological Investigations*:

A preoperative hemoglobin estimation is obtained routinely and any serious anemia corrected by adequate transfusion of whole blood or packed cells. Open heart surgery necessitates the use of heparin during the bypass, and for this reason it is important to investigate the normality of the various common factors involved in the coagulation of blood. A preoperative bleeding, clotting, and prothrombin time estimation, plus a platelet count will usually indicate any readily identifiable coagulation abnormality.

The coagulation deficits which coexist with certain cardiac lesions, such as tetralogy of Fallot for example, are expected and require no special preoperative treatment, nor do they constitute a contraindication to corrective surgery.

F. *Preoperative Care of the Cardiovascular System*:

Before surgery, as detailed an investigation of the cardiac lesion as necessary should be completed. Any heart failure present should be con-

*Winthrop Laboratories, New York 18, New York.

**A majority of patients with cardiac lesions (congenital or acquired) referred for surgical treatment have been found to have abnormally low prothrombin levels preoperatively.

trolled by suitable treatment. This complication usually responds to salt restriction, diuretics, and adequate digitalization. Routine preoperative digitalization of all patients has not been employed. Heart failure has been the indication for the use of this drug preoperatively.

G. *Preoperative Preparation of Respiratory System*:

Postoperative pulmonary complications are a source of real danger. Therefore, any effective preoperative measures taken which protect against or prevent them are of value. For some time we have made use of preoperative tracheostomy in selected patients with a recognizable reduction in pulmonary reserve.[1] A case likely to exhibit postoperative pulmonary complications is a child with left to right shunt in whom high pulmonary artery pressures together with other evidences of a high pulmonary vascular resistance are present. Normally, pulmonary compliance is lowest in infants (rigid lungs) and increases with growth through childhood and adolescence. Pulmonary hypertension further reduces pulmonary compliance; and thus increases additionally the work of breathing in these patients who as a group are characterized by weak muscular development.

Tracheostomy carries little risk and has been found to be of value because it enables those responsible for postoperative care to clear out any retained bronchial secretions or edema fluid. Also, assisted respiration using a Bennet machine is more simply managed thereby. The tracheostomy preferably should be done about a week before the intracardiac surgery so that the child can become accustomed to his altered breathing arrangement and so that any tracheal reaction secondary to the operation will have subsided. After establishment of a tracheostomy it is best to keep the child in a humidified atmosphere during this period of adaptation.

H. *Preoperative Weight*:

Accurate preoperative weighing of the patient upon several occasions and particularly just prior to surgery is important.[2] This information is necessary in order to enable one to calculate the proper volume flow during the bypass interval. It is also of great value in the estimation of the amount of blood to be replaced after surgery. Over a short period of time, i.e. during an operation, any gain or loss of weight is almost exclusively caused by alterations in blood volume.

I. *Preoperative Cut-Down for Fluid Administration and Measurement of Venous Pressure*:

We perform this in the operating theatre. This practice encourages meticulous aseptic technique. It is of value to insert the largest polyethylene tubing feasible into the vein. In adults, the cut-down may be done on the greater saphenous at the level of the ankle. In children, it is better to cut down on the saphenous at the groin in order that larger tubing can be passed into the external iliac. A slow drip of dextrose and water solution keeps this open until it is needed for the infusion of blood during the operation. The adequacy of this set-up for rapid blood replacement can be a critical factor in the success or failure of any operation.

This tubing also serves as a means for routine measuring of the venous pressure during surgery and at frequent intervals in the first two or three postoperative days. The routine measurement and recording of venous

pressure every one-half hour in cardiac patients during the immediate postoperative intervals has become as important as the ascertaining of pulse and respiratory rates, blood pressure, and body temperature. This measurement has been readily accomplished by inserting in the intravenous line a three-way stopcock connected to a saline filled manometer fixed to the bed at heart level. Any serious elevation may identify an otherwise occult bout of heart failure. An unusual lowering often indicates hypovolemia when the blood pressure hemoglobin or hematocrit are, as yet, unchanged.

The cut-down tubing is often removed within 24 hours and always within 48 to 72 hours, since this larger tubing may predispose to thrombosis or bloodstream infection if left in place for longer intervals. In the unusual patient where intravenous fluids may be required for longer intervals, administration via a needle or more peripheral cut-down is substituted.

II. *Early Postoperative Investigations and Care*:

A. *Postoperative Weight*:

Before returning the patient to the recovery room, he is accurately reweighed in the operating theatre. After allowing for the weight of any chest catheters inserted at surgery, clamps on these catheters, dressings, and perhaps an endotracheal tube, the residual value identifies any gain or loss of weight during surgery as the consequences of an altered blood volume. An example will illustrate this point. A patient weighing 14.50 kilograms immediately prior to surgery and found after the operation to measure 14.25 kilograms, has lost approximately 250 ml. of blood during the procedure. In tiny children, a far smaller deviation than this can be of crucial importance.

B. *Postoperative Blood Loss and Replacement*:

Immediately after being inserted and while the thorax is still open, the chest catheters should be placed on continuous suction to obviate stasis and clotting of blood within them. When both pleural cavities have been entered during surgery, separate reservoirs are recommended. This enables one to observe and measure the loss from each pleural space at 15-30 minute intervals (Figure 1). Furthermore, the immediate and continuous application of a pleural suction does much to avoid the development of a disastrous clotted hemothorax. All of the continuing loss is sequentially replaced volume for volume with citrated whole blood. At this point it is appropriate to emphasize the essentiality of painstaking hemostasis. Unless this is practiced unnecessary volumes of highly acid citrated blood must be reinfused. This aggravates the problem of metabolic acidosis. After the first hour or two, there should be a definite and progressive decrease in the volume of chest drainage. When this does not occur, the possibility of reopening the chest and controlling the bleeding must seriously be considered before the patient's condition has obviously deteriorated and cardiac arrest is imminent. Also, the danger is real of producing serious metabolic acidosis prevails, particularly in children when the stage has been set by anesthesia and a surgical operation with an interval of cardiopulmonary by-pass and then followed by rapid transfusion of large quan-

tities of citrated blood with a pH of 7.0 or less. A tragic level of systemic pH may then result very quickly.

A pitfall to be warned against is the assumption that a slackening in the volume of drainage invariably signifies a decrease in the amount of bleeding. Such a diminution in the quantity of blood aspirated from the pleural spaces can result from retained coagulated blood inside the chest cavity. This development tends to plug the catheters. Furthermore, this oversight results in compression of the lungs by the accumulating coagulum, and most dangerous of all, an undertransfusion of the patient, since his input of blood is being balanced only with the obvious external losses. It is possible to recognize this complication by: (1) A too abrupt decrease in chest drainage, (2) periodic auscultation and recording of the breath sounds, particularly posteriorly, (3) repeated chest radiography (Figure 2), and (4) significant alterations in the vital signs (especially venous pressure which is a sensitive index) indicating hypovolemia. It usually is best treated by immediately returning the patient to the operating room while conditions are still favorable and re-opening the wound and evacuating the offending clots, as well as achieving meticulous hemostasis of all internal oozing points.

Pre-Op. Subclavian Artery pH 7.46
Post-Op. Subclavian Artery pH 7.42

Name ..... Age ..... Hosp No. .....

Time	Chest Drainage Blood Loss				Blood				
	Left	Right	Total Both Chest	Run Total	Added to I.V.	Taken I.V.	Hgb.	Urine Output & pH	Blood Chem
2 p.m.	Specimen			20 cc.	100		12.5		NA 142 K 4.1
3 p.m.	15	20	35	55 cc.					CO. 20 Cl 91
3:30	10	15	25	80	100	100			
4:30	13	20	33	113					
5:30	10	20	30	143				200 cc.	
6:30	8	15	23	166					
7:30	5	15	20	180		80			

FIGURE 1: Chart on which postoperative blood loss and blood replacement are routinely recorded. The data recorded are from a representative case record of a 4 year old child undergoing a 52 minute perfusion (helix reservoir bubble oxygenator) for complete correction of the tetralogy of Fallot defects. This record is usually kept in a detailed fashion until the morning after surgery. By that time chest drainage is serous and less frequent measurements suffice. NOTE: To obviate errors blood is added to the intravenous flask in 100 cc. increments, even for adults, and recorded both when added and again when actually taken.

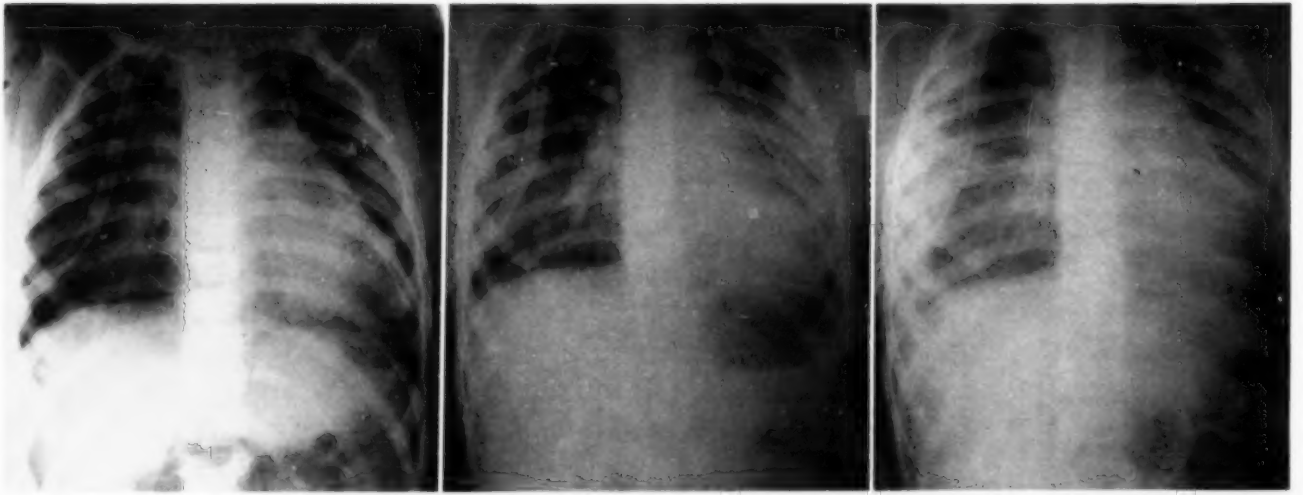

FIGURE 2A FIGURE 2B FIGURE 2C

Figure 2A: Chest x-ray of patient on return to the post-anesthesia recovery room.—*Figure 2B:* A sudden diminution in drainage from right chest occurred. Chest radiography reveals slight haziness of right lung field. This is the earliest sign of accumulating hemothorax.—*Figure 2C:* Chest radiography half an hour later shows definite accumulation of blood in the right chest.

C. *Care of the Respiratory System*:

Certainly invaluable help is provided through well-taken portable chest x-rays in the early and subsequent postoperative phases by identifying the presence of atelectasis or pneumothorax. We have found that if these are taken in the supine position, excellent films can be obtained with less disturbance to the patient. Constant vigilance is also needed by the attending nurses and surgeons lest they become totally dependent on these periodic checks through roentgenograms. Painstaking care of the respiratory system in the postoperative period is of utmost importance, especially in the smaller children where definite physical limitations exist in the tracheobronchial tree. The diameter of the larynx and trachea are so small that obstruction from edema and foreign material occurs easily. These handicaps are magnified by decreased expiratory excursions due to abdominal distension, the thoracotomy wound, and physical exhaustion due to lessened muscular development often coupled with decreased pulmonary compliance. Under such circumstances, without scrupulous observation and care, some pulmonary complication and usually a serious one is prone to arise due to the almost inevitable retention of bronchial secretions. To keep the respiratory tract free is to save tots who would otherwise be lost.[3, 4]

The use of median sternotomy, whenever applicable, has reduced the frequency and severity of postoperative pulmonary complications.

1. *Clearing of the Mouth, Trachea, and Hypopharynx.*

This should be thoroughly done by the anesthesiologist immediately after the operation and before the endotracheal tube is removed. Although this maneuver must be carried out, it is important that each time the trachea and its major ramifications are aspirated that these movements be quickly and expeditiously performed. Prolonged continuous effort directed at extracting the ultimate drop of mucous is a severe strain on the child and can prove fatal. Periodic intermittent attempts are safer. A suction apparatus should be constantly available in the recovery room for the immediate removal of any secretions which collect in the pharynx. This and the trachea are to be suctioned under direct vision whenever necessary, observing the precautions cited above. In patients with large quantities of bronchial secretions, or considerable edema fluid, the advantages of a tracheostomy are certain to be appreciated and the surgeon should not hesitate to create a tracheostomy at any time postoperatively if this seems indicated on the aforementioned basis.

2. *Decompression of the Gastrointestinal Tract.*

Distension of the stomach will interfere with the respiratory movements, and should, therefore, be corrected. This can be done usually by aspirating the contents intermittently and then removing the tube each time. In others, constant indwelling decompression of the stomach is necessary. The latter has the added advantage of eliminating the risk of aspirating vomitus. It carries, however, the drawback of narrowing the airway of the oro-nasal pharynx and is likely to increase the volume of secretion from this area.

3. *Posture.*

Frequent turning of the child from side to side by those in attendance

helps to aerate the lungs and to resolve patches of atelectasis and other reversible consolidations.

4. *External Environment.*

Oxygen.

For infants it is desirable to create a properly warm, humid atmosphere, enriched in oxygen content. For others some enhancement of the oxygen content can be brought about by use of a nasal catheter or some form of oxygen tent. However, it is unlikely that this often adds a great deal of oxygen to the respiratory uptake. A tracheostomy with a cuffed tube, on the other hand, can be connected directly to a breathing apparatus supplying oxygen in any percentage desired up to 100 per cent. This represents one more dividend accruable through use of this supplementary operation.

Humidity.

Patients likely to develop pulmonary complications handle their secretions more readily in an atmosphere laden with water vapor containing a detergent (Tergemist)* and fortified by an antibiotic such as neomycin. Augmentation of the humidity can be obtained by bubbling the oxygen supply through water or by the use of cold air humidifiers. A high vapor

FIGURE 3: Patient in recovery room with tracheostomy tube connected to the intermittent positive pressure (Bennett type) respirator. Chest catheters are attached to a controlled suction apparatus. Note also the specially designed recovery room carts which facilitate patient transport and care.

*Abbott Laboratories, North Chicago, Illinois.

content will assist in decreasing the tenacity of the bronchial secretions so that they can be raised or aspirated more readily.

5. *Use of Ancillary Respiratory Apparatus.*

In the immediate postoperative interval the minute ventilation volume is repeatedly measured and recorded in all of those patients deemed likely to have a lessened pulmonary reserve. Whenever the ventilation volume is found to be low, immediate steps are taken to ascertain the cause (secretions, atelectasis, pneumothorax, fatigue) and corrective measures instituted.

Inadequate depth to the patient's breathing can be assisted whether this stems from patient weakness or decrease in pulmonary elasticity by connecting the patient's tracheostomy tube directly to a Bennett-type machine* or a comparable ventilatory device for intermittent positive pressure breathing. At times the completely automatic units, as distinguished from the above demand respirators, have been of help.

These measures have been extremely valuable in preventing sudden cardiac arrest due to the insidious onset of respiratory acidosis.

D. *Parenteral Fluid Therapy*:

(a) *Total Fluid Balance*: It is well to aim at keeping the patient slightly dehydrated in the early postoperative period. The potential dangers of overhydration far exceed those attributable to moderate dehydration. The latter state minimizes the risk from pulmonary edema. We generally calculate the volume to be infused in the first 24 hours based on an insensible loss of 1.0 cc./Kg. of body weight/hour supplemented by an allowance for urinary volume depending on the patient's size. On this score, it is safe to give during the operation, and for the first 24 hours, a fluid whose composition approximates that in Mead's No. 48 solution** at a rate of 2½ ml./kilo./hour. The next day, fluids can usually be accepted (and retained) by the oral route, and further intravenous fluids are unnecessary.

(b) *Electrolytes*: The blood levels for sodium, potassium, chloride, and carbon dioxide combining power together with the arterial pH are determined immediately following the operation. Serious shifts in the electrolyte pattern are not common then, nor are they likely to occur in the usual convalescent, since the patient ordinarily can tolerate fluids by mouth after the first 24 hours.

1. *Sodium Chloride*

When the patient has been on a low salt diet for months preceding surgery, particular care is required. Even modest volumes of salt free fluid in this type of case can result in water intoxication. In fact, among children, convulsions can be induced with the rapid administration intravenously of but a few hundred cubic centimeters of 5 per cent dextrose in water. On the other hand, overloading the circulation with salt can precipitate cardiac failure and pulmonary edema. The intravenous infusion

*V. Ray Bennett & Associates, Inc., Los Angeles 48, California.

**Mead Johnson & Co., Evansville 21, Indiana. Mead's No. 48 solution contains 48 milliequivalents total of sodium, potassium, magnesium and an equal quantity of chloride, lactate, and phosphate in a 5 per cent dextrose solution.

of a dilute electrolyte solution (as mentioned above) has proven a workable means of avoiding these complications, particularly when the total volume provided intravenously is kept on the "dry side."

2. *Potassium:*

The postoperative serum potassium levels[5, 6] are usually within normal limits or slightly reduced secondary to hyperglycemia. It has rarely been necessary to supplement the potassium intake beyond that contained in the Mead's 48 solution. A precaution to be observed, however, is the increased activity of digitalis preparations in the presence of a low serum potassium value. Rapid intravenous digitalization under these circumstances can prove harmful or even fatal. Assuredly, also any addition to the potassium intake should be avoided when the urine output remains low.

Moreover, if for any of a variety of possible reasons the cardiac output is low in the immediate postoperative period (acute forward failure*) the serum potassium may rise rapidly and reach toxic levels within even a few hours due to a combination of abnormal release of intracellular potassium (tissue hypoxia), and inadequate renal clearance. Concomitantly, a metabolic acidosis is inevitably associated with this reduced cardiac output. Obviously, the only sure way to manage this serious situation with complete success is by restoration of the cardiac output to adequate levels before cardiac arrest occurs. Depending upon the etiology this may or may not be possible, but we have now upon a number of occasions recognized this syndrome in time to undertake successful management by one or more of the specific measures mentioned under Care of the Respiratory System (above) or under Care of the Cardiovascular System (below).

In order to gain the time often necessary to diagnose and institute therapy for the basic problem at hand, there are several things that can be done as emergency measures. It is emphasized that these are for the most part symptomatic treatment to gain time, and only in exceptional instances will they be successful in themselves. These measures are use of vasopressors (Levophed, Aramine, Vasoxyl) intravenous 20 to 50 per cent glucose, enemas of ion exchange resins to lower potassium, sodium bicarbonate intravenously for pH changes, Isuprel (Isoproterenol HCl) intravenously or rectally to increase myocardial contractility and to improve output, respiratory assistance via an endotracheal tube, or tracheotomy for ventilation problems.

3. *pH of the Blood*:

A tendency toward metabolic acidosis is created in patients who have undergone a period of cardio-pulmonary by-pass. Some patients, particularly those with cyanotic heart disease, may have an uncompensated metabolic acidosis[5] preoperatively. This tendency is increased when duration of anesthesia or the period of cardio-pulmonary by-pass or both are pro-

*Some common causes of this syndrome are: complete atrioventricular dissociation, myocardial insufficiency secondary to a long interval of hypoxia with potassium arrest, some residual obstruction remaining after correction of pulmonic stenosis either in patients with an intact ventricular septum or in tetralogy patients in whom the ventricular septum has been closed, severe obstructive changes in the pulmonary arteriolar bed associated with advanced pulmonary hypertension.

longed. In this case, intravenous sodium bicarbonate can be added to the patient's postoperative infusate from time to time observing the blood pH and urine until more nearly normal values have been secured. Necessarily the total amount of sodium that can be injected is limited, but in the absence of other causes for prolonging the metabolic acidosis postoperatively, the internal milieu rapidly returns to a safe equilibrium and the use of bicarbonate therapy is rarely necessary. Severe acidosis continuing well into the postoperative period is dangerous and may lead to a decreased efficiency in cardiac action and an increased tendency toward cardiac arrest.

It is worthy of emphasis that where a severe acidosis, either of respiratory or metabolic origin, is secondary to some other primary cause (low cardiac output, inadequate renal function) it has been impossible to achieve more than very temporary and evenescent benefits by use of even heroic quantities of sodium bicarbonate intravenously because the acid radicals are being produced by the body tissues much faster than they can be neutralized or excreted. Thus, bicarbonate therapy is of value largely to gain time while more specific therapy is instituted.

It should also be borne in mind that sodium lactate is of negligible value in the treatment of acute acidosis because the pH of the solution is neutral and the lactate must be metabolized before the alkalinizing effects are exerted. Metabolism of the lactate may not be possible in time to help such patients with a depressed circulation.

E. *Care of the Cardiovascular System*:

Overloading of the circulation with unnecessary volumes of blood in the postoperative period is to be avoided. This state can be detected by a rise in the venous pressure. An accurate recording of this is obtainable merely by connecting the cut down to an appropriate manometer via a three way stopcock. During the first 24-48 hours the venous pressure is charted regularly along with the other vital signs (pulse, blood pressure, respiratory rate, and temperature) (Figure 4). This check, together with observation of the neck veins, are important points in the immediate postoperative interlude.

Myocardial failure inexplicable (at times) and abrupt in onset may develop in this period. Its appearance is a definite indication for prompt digitalization. Bouts of sinus tachycardia may also create a strain on the circulatory system. When this occurs in the absence of other obvious causative factors, prompt digitalization is indicated.

Complete Atrioventricular Dissociation:

Fortunately, this previously ominous and often lethal complication of open heart surgery for repair of septal defects can now be well managed by insertion of a myocardial electrode to allow direct myocardial stimulation from a suitable pacemaker. By this means the heart rate (and cardiac output) can be readily maintained at desired levels until such time as sinus rhythm returns or sufficient adaptation to the slower rate has had time to take place. The techniques and methods for use of the myocardial electrode and transistorized battery activated pacemaker have been dealt with more fully in previous publications.[7, 8, 9]

For an occasional patient with postoperative complete heart block, the heart rate may be adequately controlled by the internal pacemaker stimulation but there may be definite evidences of an inadequate cardiac output without otherwise satisfactory explanation. Nearly always this situation will be seen in a patient in whom there was recognized severe myocardial strain and a low cardiac reserve before corrective surgery. In addition, the myocardiopathy may have been aggravated by a period of potassium arrest at surgery. In such a patient digitalization is indicated and even though complete heart block is present there is no contraindication to the judicious use of digitalis when pacemaker stimulation is in effect. Another drug that has been of distinct value in such a patient, either alone or combined with digitalis, has been Isuprel (Isoproterenol HCl) which increases cardiac contractility.

If three or four weeks have passed and the patient still remains in complete atrioventricular dissociation, the individual may be weaned over a period of several days or more by gradually decreasing the rate of the

FIGURE 4: Chart showing vital signs regularly recorded postoperatively.

stimulation and progressively increasing the dose of Isuprel administered sufficient to maintain a satisfactory cardiac output. In general, we have found that rectal Isuprel[10] has a more prolonged, and appears to have a more potent, effect than that administered sublingually. The rectal route of administration for Isuprel also has the advantage that it does not require the cooperation of the infant or smaller child.

It is usually advisable to connect the patient to a heart rate monitor at the time pacemaker stimulation is stopped. Any abrupt and possibly lethal reversion to a severe bradycardia is obviated by these means, for its appearance can be fatal in the early postoperative period unless immediately detected and treated.

F. *The Patient's Temperature*:

Open heart surgery, particularly in children, often induces a fall in the body temperature. The drop may be as large as 10 degrees Fahrenheit. This degree of hypothermia persisting after the patient comes off of total by-pass increases the danger from ventricular fibrillation. Prophylaxis against this occurrence is most effectively obtained by placing the patient on a warming blanket maintained at no higher than 110 F. The warming unit of a Thermo-Rite machine has been used satisfactorily for this purpose. In the postoperative period any great swings upward in temperature are likewise to be avoided for the work of the heart is increased thereby. Any tendency for such should be damped by appropriate cooling measures utilizing the Thermo-Rite mattress.

G. *Antibiotics Postoperatively*:

The dangers from bacterial infection, and particularly endocarditis, looms prominently before the surgeon after an open heart operation. Antibiotics in adequate doses for preventive treatment should be used, therefore, regularly. We routinely prescribe parenteral injections of penicillin and streptomycin if no sensitivity for them is present. In fact, an initial intravenous dose of penicillin is given while the patient is still on the operating table. Thereafter, these drugs are continued for approximately 10 days. If a wound infection occurs, the causal organism should be cultured and sensitivity tests carried out to determine the appropriate antibiotics.

H. *Sedation*:

Although excessive pain and unceasing restlessness need be controlled, a greater danger lies in giving sedation to the point of hindering full respiratory movements. Restlessness, mental confusion and anxious facies bespeak progressive hypoxia, and the administration of sedatives under these circumstances is likely to be fatal. Rather, respiratory assistance by one of the previously mentioned methods is urgent. Moreover, deep sedation dulls the cough reflex, and hence increases the dangers of pulmonary complications. Therefore, in general, none or a light level of sensory depression by drugs is more advantageous, albeit less pleasant, for the patient.

I. *Dressings and Intrapleural Drainage Tubes*:

The initial dressing is a light one which consists of but a few fluffs,

moistened in aqueous zephiran, and is scantily fastened to the chest wall with elastic tape. An occlusive compression-type covering likely to hamper free respiratory excursion should be rigorously avoided. The dressing is not disturbed until skin sutures are taken out at about 9-11 days.

Intrapleural drainage tubes are removed as soon as drainage falls to a relatively limited volume each 24 hours, i.e., less than 50 cc. Rarely serum will collect in the pleural cavity after removal of the tubes and require aspiration.

III. *Late Postoperative Care*:

A. *Bed Rest*:

The patient is usually kept in bed for about 3 to 5 days. Then gradually he is allowed to be ambulatory. Should heart failure appear thereafter, a return to bed rest is indicated. Other complications such as complete heart block may delay the patient's return to the ambulatory state.

B. *Diet*:

The temporary appearance of heart failure may occur anytime postoperatively up to 21 days due to the traumatic myocarditis engendered by the cardiotomy. The prognosis is usually good since its course is self limited, especially if it is promptly recognized by various means including careful weighing of the patient which reveals occult water retention, and identifies the need for restriction of the salt intake, use of appropriate diuretics and a re-evaluation of the digitalization status.

SUMMARY

The important aspects in the pre and postoperative care of patients undergoing open heart surgery based upon our experience at the University of Minnesota Variety Club Heart Hospital with more than 700 patients are discussed.

The careful preparation of the operative field with phisohex and the preoperative use of antibiotics and a good diet supplemented by vitamins will assist in obtaining smooth convalescence free of infections and complications.

Patients with a high pulmonary flow or pulmonary congestion are prone to infections of the tracheobronchial tree and lungs and should be adequately treated before surgery.

Overt or incipient heart failure should be treated with salt restriction, diuretics, and digitalization, but routine preoperative digitalization is not recommended.

Tracheostomies are performed preoperatively in patients with high pulmonary artery pressures and resistances to enable one to deal more adequately with secretions postoperatively and to assist respiration in this period if necessary.

Accurate preoperative weight should be obtained just before induction of anesthesia to enable one to calibrate the change in blood volume when compared with the immediate postoperative weight.

In the immediate postoperative phase, careful measurement and replacement of blood loss from the chest catheters and care of the tracheobronchial tree are some of the most important aspects leading to a low mortality.

Clearing of secretions from the mouth, nasopharynx, and hypopharynx by careful suctioning is recommended. Oxygen and humidity often supplemented with bronchial detergents are used routinely.

Unless there are unusual losses, electrolyte imbalance is not a problem in the postoperative phase. Intravenous fluids should be limited to 1½ to 2 cc./Kg./hour for the first 24 hours to minimize the risk of pulmonary edema. Enough sodium chloride is given to cover losses due to gastric suction and sweating.

Prevention of acidosis in the postoperative period is of greatest importance. An adequate circulation is the most important single factor in the prevention of this grave complication, however, control of restlessness and high temperatures and the use of sodium bicarbonate will be of some help.

Heart failure should be treated in the usual manner postoperatively. Temporary cardiac decompensation that occurs 10-14 days after surgery due to the traumatic myocarditis is seen occasionally especially in patients with low cardiac reserve preoperatively. This is detected early by following daily weights and responds well to digitalization, salt restriction, and in no way jeopardizes an ultimately good prognosis if properly managed.

The treatment of heart block is managed with a myocardial (internal) electrode and artificial pacemaker constructed to give the small voltages necessary (1-10 volts). Isuprel is occasionally utilized to supplement the pacemaker and facilitate reconversion to a sinus rhythm.

Antibiotics are used for 10-12 days postoperatively.

The patients are discharged 14-21 days after surgery.

RESUMEN

Se discuten los aspectos importantes en el cuidado pre y postoperatorio de los enfermos que se sujetan a cirugía a corazón abierto, basándose en nuestra experiencia en el Hospital Cardiológico del Variety Club de la Universidad de Minnesota con más de 700 enfermos.

Para obtener una buena convalescencia libre de infecciones y complicaciones es una ayuda la preparación del campo operatorio con phisohex, el uso preoperatorio de antibióticos y una buena alimentación con vitaminas suplementarias.

Los enfermos con elevadas cantidades de secreciones o con congestión pulmonar son más inclinados a tener infecciones del árbol traqueobronquial y de los pulmones y deben ser tratados convenientemente antes de operarse.

La insuficiencia cardiaca franca o incipiente debe tratarse por la restricción de sal, diuréticos y digitalización, pero la digitalización preoperatoria como rutina no es recomendable.

En los enfermos con elevada presión de las arterias pulmonares se recomienda se haga la traqueostomía preoperatoria para permitirles expulsar más fácilmente las secreciones después de la operación y ayudar a la respiración en este período si se necesita.

Debe tomarse el peso con exactitud antes de la inducción de la anestesia para permitir la calibración del cambio de volumen sanguíneo cuando se compara con el peso inmediatamente después de la operación.

En la fase postoperatoria inmediata, una medición cuidadosa y substitución de la sangre perdida a través de los catéteres y el cuidado del árbol traqueobronquial, son de las cosas más importantes.

La limpieza de secreciones de la boca, de la nasofaringe, e hipofaringe por succión cuidadosa se recomiendan. Se usan como recursos de rutina oxígeno y humedad con detergentes bronquiales.

A menos que haya pérdidas inacostumbradas, el desequilibrio de los electrolitos no es un problema en el postoperatorio. Los líquidos intravenosos deben limitarse a 1½ a 2 c.c. por kilogramo por hora por las primeras 24 horas para disminuir el riesgo del edema pulmonar.

Se da bastante cloruro de sodio para cubrir las pérdidas debidas a la sudoración y a la succión gástrica.

La prevención de la acidosis en el período postoperatorio es de la mayor importancia. Una circulación adecuada es el factor único de mayor importancia de esta grave complicación, sin embargo, el control de la inquietud y de las temperaturas elevadas y el uso del bicarbonato de sodio son de alguna utilidad.

La insuficiencia cardiaca debe tratarse de la manera habitual preoperatoriamente. La descompensación cardiaca temporal ocurre de 10 a 14 días después de la cirugía debida a miocarditis traumática, y es vista ocasionalmente en enfermos con baja reserva cardiaca preoperatoria. Esto es descubierto tempranamente por las pesadas diarias, y responde bien a la digitalización, restricción de sal, y de ninguna manera pone en riesgo un pronóstico favorable si se trata adecuadamente.

El tratamiento del bloqueo cardiaco es hecho con un electrodo miocárdico (interno) y un marcador de paso artificial construído para dar los pequeños voltajes necessarios (a-10 volts).

El isuprel esocasionalmente usado para suplementar el marcador de paso y facilitar la reconversión a un ritmo sinusal.

Los antibióticos se necesitan por 10 a 12 días después de la operación. Los enfermos se dan de alta de 14 a 21 días después de operados.

ZUSAMMENFASSUNG

Die wichtigsten Erfahrungen in der pre- und post-operativen Behandlung von mehr als 700 Patienten, die offene Herzchirurgie an der Universität von Minnesota, im Variety Club Heart Hospital gehabt haben, werden dargestellt.

Da die Operationen meisten keinen dringlichen Eingriff erfordern, soll man sich Zeit lassen, um dem Patienten in den bestmöglichsten Gesundheitszustand zu bringen. Die sorgfältige Vorbereitung des Operationfeldes mit Phisohex und der preoperative Gebrauch von Antibiotica und eine gute Diät mit Vitaminzugabe sind ratsam, um eine möglichst komplikationsfreie Rekonvaleszenz zu haben.

Besondere Aufmerksamkeit sollte man den oberen Luftwegen schenken. Patienten mit hohem Pulmonaldruck oder Lungenveränderungen neigen besonders zur Infektion der Luftwege und Lungen. Solche Komplikationen sollten vor der Operation entsprechend behandelt werden.

Offensichtliche oder drohende Herzdecompensation wird durch Ein-

schränkung der Kochsalzzufuhr und mit Diuretica sowie Digitalisierung behandelt. Aber eine routinmässige Vorbehandlung mit Digitalis wird nicht unbedingt empfohlen.

Tracheotomien werden bei Patienten mit hohem Druck in der Arteria pulmonalis bereits vor der Operation durchgeführt, um der vermehrten Sekretion im postoperativen Verlauf Herr zu werden und die Atmung wenn notwendig zu unterstützen. Das ist wichtig, da aus einer Gewichtsänderung nach der Operation auf eine Änderung im Blutvolumen geschlossen werden kann.

In der unmittelbaren postoperativen Phase ist eine sorgfältige Messung des durch die Pleura-Catheter abgesaugten Blutes sehr wichtig. Die entsprechende Menge sollte sofort wieder ersetzt werden. Ausserdem ist den Luftwegen besonders Aufmerksamkeit zu schenken.

Das Absaugen von Sekret aus Mund, rasopharyngeal- und Hypopharyngealraum ist notwendig. Mit Feuchtigkeit angereicherter Sauerstoff und häufig gar Zusatz von Inhalationsmedikamenten wird regelmässig angewandt.

Der Elektrolythaushalt bereitet meistens keine Schwierigkeiten postoperativ. Nicht mehr als $1\frac{1}{2}$ bis 2 cc./kg. stunde werden als intravenoese Flüssigkeit in den ersten 24 Stunden gegeben, um einem Lungenoedem vorzubeugen. Genug Kochsalz wird je nach Verlust durch Magensonde und Schweiss zugesetzt.

Am wichtigsten im postoperativen Verlauf ist die Verhütung der Acidose. Eine ausreichende Blutzirkulation ist der wichtigste und einzige Faktor zur Verhütung dieser Komplikation. Behandlung der Ruhelosigkeit des Patienten und der hohen Temperaturen sowie der Gebrauch von Natriumcarbonat können von gewissem Einfluss sein.

Entstehende postoperative Herzdekompensation wird in üblicher Weise behandelt. Eine vorübergehende Dekompensation, die etwa 10-14 Tage nach der Operation als Folge der traumatischen Myocarditis auftritt, sieht man gelegentlich, insbesondere aber bei Patienten mit geringer Herzreserve. Durch tägliche Überprüfung des Körpergewichtes kann dies rechtzeitig erkannt werden und ist einer Behandlung mit Digitalis und Salzeinschränkung gut zugänglich. Die Prognose ist gut bei sorgfältiger Überwachung des Patienten.

Bei Patienten mit Herzblock wird eine ins Myocardium genähte Elektrode mit dem künstlichen "Pacemaker" verbunden, der die nötigen (1-10) Volt erzeugt. Wir verwenden gelegentlich Isuprel zur Unterstützung des "Pacemaker," um die Wiederherstellung des Sinusrhythmus zu erleicherten.

Antibiotica werden 10-12 Tage lang postoperativ verabreicht.

Die Entlassung des Patienten erfolgt 14-21 Tage nach der Operation.

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The Treatment of Acute Infectious Pericarditis and Chronic Constrictive Pericarditis

Chronic constrictive pericarditis may be the end result in the healing of acute infectious pericarditis by the formation of granulation tissue in the pericardial cavity gradually contracting and forming a firm scar, encasing the heart and interfering with its filling.

It usually results from either tuberculosis or pyogenic infection and only rarely may it follow rheumatic pericarditis. It is questionable if it ever results from recurrent idiopathic pericarditis. However there is a case[1] reported in the literature where it is alleged to have done so although absolute proof is lacking.

Trauma to the heart with its resulting hemo-pericarditis may also produce constrictive pericarditis.[2, 3]

The treatment of the acute form of this disease will be reviewed and it will be indicated where a relationship to chronic constrictive pericarditis exists and in what way it may be prevented.

Acute Non Specific "Idiopathic" pericarditis is a benign disease. Its treatment is important, however, because frequently at the onset of this disease it has been confused with acute myocardial infarction. It has become a common practice to use anticoagulant therapy promptly in the treatment of myocardial infarction and if inadvertently anticoagulant drugs should be administered to a patient with idiopathic pericarditis serious complications and even death from cardiac tamponade may ensue. Two cases [4, 5] have been reported where this has happened.

A new test has been reported by Fremont[6] and others, the fibrinogen polymerization test, which may be helpful in distinguishing non-specific pericarditis from myocardial infarction. They found that this test is positive in non-specific pericarditis and myocarditis while on the other hand it is negative in patients with coronary artery disease and tuberculous pericarditis.

Most cases of non-specific pericarditis can be treated symptomatically.[7] They should remain in bed until all signs of activity of the disease has subsided. Antibiotics have been used in the treatment[8, 9] but other authors are of the opinion that they are of no specific value.[10, 11]

Corticotropin and cortisone have been given in the treatment of patients that were seriously ill with the disease[12-15] and in all but one instance[16] the course of the patient's illness promptly improved. When cortisone was discontinued one patient suffered a relapse[17] and responded when the drug was resumed and remained well after it was gradually discontinued.

It is thought that steroid therapy [13] may be effective in this disease as it suppresses inflammatory reaction during the acute phase of the illness but does not alter the natural course of the disease. It is recommended in the treatment of severely ill patients in dosages of 25 mgm. to 50 mgm.

of cortisone four times a day or prednisone 10 to 15 mgm. four times a day.

Dressler[18] has noticed a striking resemblance between the clinical and laboratory features of idiopathic pericarditis and those of post commissurotomy or post-cardiotomy syndrome. Both diseases include pericarditis, pleurisy, and pneumonitis, although the incidence of these components varies in individual cases. The outstanding features are pain of the pleuro-pericardial type and fever. Both syndromes usually run a benign course and tend to relapse frequently.

The same series of events, namely, pericarditis, pleuritis, and pneumonitis have been described by Dressler[19] as a complication of myocardial infarction and are known to respond to steroid therapy.

Dresdale and others[20] have reported the use of cortisone in doses of 50 to 300 mgm. daily during 65 episodes of P.C.S. in 21 patients and found that there was a complete remission of the clinical findings within 24 to 36 hours in 62 instances. Two patients that did not respond to 50 mgm. of cortisone daily finally remitted promptly on 200 mgm.

In as much as cortisone and its related products are so effective in controlling syndromes clinically and symptomatically similar to acute idiopathic pericarditis they should be tried promptly in this disease in an effort to see whether they will influence its course.

Acute Rheumatic Pericarditis which is commonly associated with other evidences of severe rheumatic infection may occur either as the fibrinous (dry) type or the serofibrinous (wet type).

Patients with the serofibrinous type should be carefully watched for the development of cardiac tamponade which would constitute an urgent indication for parencentesis of the pericardium.[21]

This procedure should not be undertaken without definite indications as there is a definite risk involved. Fatal tears of the myocardium have occurred. A coronary or internal mammary artery may be injured or a state of shock or a cardiac arrythmia can be induced reflexly. The patient should be prepared by the administration of a narcotic plus atropine.

Several routes have been advocated. The apical is particularly safe when the apex beat is detected well within the left border of cardiac dullness. The subxyphoid approach is probably the safest.

The patient is lying semi-upright with the spine supported in marked extension by pillows. The needle should be made the exploratory electrode of an electro-cardiographic machine by attachment to the precordial lead, with the leads to the central terminal being connected in the usual manner. An assistant may then note immediately the contact of the needle with the myocardium since instant displacement of the S-T segment will occur. After the fluid is aspirated air may be introduced into the pericardial sac since this may provide information by X-ray as to the thickness of the parietal layer, the presence or absence of adhesions and the actual size of the heart. The placing of air also may be of therapeutic value as it is believed to inhibit the development of adhesions.

The treatment of rheumatic pericarditis is that of rheumatic fever in general except that when signs of pericarditis are present massive salicylate therapy in doses of 6 to 10 grams in 24 hours either administered in four oral doses or by rectal instillation twice a day is usually effective.

However in the presence of heart failure acetyl salicylatic acid is preferred to the sodium salt.

Recently steroids have been used in the treatment of rheumatic pericarditis but there is no evidence that they are any more effective than massive doses of salicylates.

Rheumatic pericarditis rarely causes constrictive pericarditis[22] but it sometimes leads to the development of chronic adhesive mediastino pericarditis.

Acute Pyogenic Pericarditis. In recent years the use of antibiotics has greatly altered the incidence and treatment of purulent pericarditis whereas once the condition was a frequent complication of pneumococcal pneumonia, staphylococcus septicemia and meningococcemia, it now rarely proceeds to this stage. Before 1941 Strieder and Sandusky[23] estimated the mortality to be 100 per cent in untreated cases. They were able to reduce the mortality to 50 per cent when pericardostomy was performed. Since the advent of antibiotics the mortality has been markedly reduced.

Once pericarditis is suspected clinically and radiographically, aspiration is the only means of confirming the diagnosis.[24] The anterior apical or subxyphoid routes as described earlier in the article are preferred. Frequently the latter route should be used to prevent contamination of the left plural cavity. Once the purulent exudate is encountered all pus should be withdrawn relieving the tamponade and lowering the risk of surgery. Culture and sensitivity studies should be determined on this material to properly identify the organism so that the appropriate antibiotic therapy may be instituted. Systemic antibiotic therapy cannot be depended upon entirely so local instillation of antibiotic solution is employed. Usually the case can be handled successfully by pericardiocentesis and antibiotic therapy with local instillation into the pericardium. However with signs of uncontrolled infection or persistent cardiac tamponade and also because of the danger of repeated aspiration, surgical drainage is indicated. Occasionally the purulent exudate becomes thick and lobulated excluding the possibility of evacuation by irrigation. This problem can be overcome by the instillation into the pericardial cavity through a catheter of a solution containing 100,000 units of streptokinase*[25] and 25,000 units of streptodonase and an appropriate antibiotic.

The enzyme by lysing fibrin and digesting the waste products of the exudate liquefies the material and promotes drainage.[24] There are several reports in the literature where this method of treatment has been used successfully.[26-29] Unless pyogenic pericarditis is promptly and adequately treated it can lead to the production of constrictive pericarditis.

The Treatment of Tuberculous Pericarditis as suggested by Col. Gayette and his associates[30] should consist of bed rest, chemotherapy and aspiration of the pericardium for diagnosis and, or, relief of tamponade.

Initially chemotherapy should consist of 2 grams of streptomycin every third day and the daily administration of 12 grams of para-aminosalicylic acid and/or, isoniazid, 300 to 400 mgms. daily. Every patient in this series received this therapy for a minimum of 120 days but preferably for 8 to 12 months.[30] The actual duration of the therapy depends upon the response of the patient and it is given preferably for 6 months after

*The commercial product prepared by Lederle Laboratories is known as "Vardase".

all signs of activity of the disease have ceased. The criteria for inactivity are, 1, patient is afebrile, 2, a normal sedimentation rate. 3, there is no evidence of congestion. 4, heart is normal in size with normal pulsation, and 5, stable electrocardiogram. These authors believe that when the diagnosis of tuberculous pericarditis is reasonably certain on clinical grounds, treatment should be instituted as soon as the initial studies have been completed and not withheld pending the results of cultural studies or animal inoculation. They state that six weeks of chemotherapy is a benign form of treatment. In the event that the diagnosis ultimately proves to be erroneous no harm has been done and if the diagnosis is later confirmed valuable time has been gained.

Twenty-seven patients with primary tuberculous pericarditis were treated with intermittent streptomycin, para-aminosalicylic acid or isoniazid and treatment was successful in 21 of them and unsatisfactory in six. Constrictive pericarditis developed in five. One died following surgery and another one with overwhelming tuberculous infection.

Chemotherapy should be instituted early and should include streptomycin, para-aminosalicylic acid and or, isoniazid and should be continued for at least six months after all signs of activity have ceased.

If the patient fails to respond in spite of adequate therapy and signs of congestion persist or progress, he should be subjected to prompt surgical resection, even though active disease is present. Chemotherapy should be continued through the operative period and preferably for six months thereafter.

In most cases of chronic pericarditis the etiology may not be apparent but is suspected of being tuberculous in nature. Available diagnostic procedures are extremely limited and a presumptive diagnosis alone often has been the basis for treatment. In bacterial pericarditis the findings on examination of the pericardial fluid may be diagnostic but in tubercular pericarditis the findings on direct smears, culture and guinea pig inoculation of the specimen of fluid often are negative. Histopathological and bacteriologic examination of the diseased pericardium itself may be of considerable assistance in selective cases.

A technique of pericardial biopsy is described[31] and has been performed in a series of 22 cases. Pericardial biopsy permitted direct visualization within the pericardial sac. Histopathologic examination and culture of the diseased pericardium and fluid may establish the etiology of chronic pericarditis and treatment on this basis may be more accurately administered.

Pericardial biopsy has also been used in establishing the diagnosis in acute pericarditis when other diagnostic procedures have failed and in a case reported by Barr[32] it was the only way the diagnosis could be confirmed as tuberculous pericarditis and prompt treatment instituted.

Chronic Constrictive Pericarditis: Richard Hill[33] and his associates draws our attention to the fact that the clinical findings of chronic constrictive pericarditis may simulate those of decompensated portal cirrhosis. The predominance of hepatomegaly and ascites and the absence of orthopnea may direct attention away from the heart and toward the liver. Since chronic constrictive pericarditis is so successfully treated surgically the importance of recognizing the entity is obvious. In 16 patients in whom

chronic constrictive pericarditis caused some confusion with primary disease of the liver the correct diagnosis was suspected in all when objective evidence of elevated venous pressure was sought. Therefore in patients with massive ascites particularly if they have nonedematous legs and normal values for serum albumin, it is fundamental to look for clinical signs of elevation of venous pressure by direct measurements of the pressure in anterior cubital vein.

When it has been determined that a patient with ascites and hepatomegaly has an elevated venous pressure chronic constrictive pericarditis is a likely diagnostic possibility. Further studies including fluoroscopy, electrocardiograms, and cardiac catheterization may confirm the diagnosis.

In constrictive pericarditis surgical decortication is the treatment of choice. In a review of 72 cases of pericardial constriction by Cooley and others[34] in which operation was performed at the Mayo Clinic in 21 years ending in 1955, excellent operative results were obtained of twenty-eight patients undergoing pericardiectomy after 1950, 25 have had good results and there were three operative deaths.

Burwell[35] in an editorial in "*Circulation*" in 1957 states that patients with constrictive pericarditis if not treated by surgical therapy show little tendency to improvement and tend to deteriorate gradually over the years. On the other hand most patients with constrictive pericarditis who are operated upon are improved and may return to normal or nearly normal activity.

In Burwell's experience[35] the degree of success realized from operation is determined chiefly by the following factors which he enumerates as follows: 1. The type and extent of operation and the degree to which it has been possible to remove the constricting scar from the ventricles. 2. The presence or absence of continued activity of the causative infection. 3. The extent to which myocardial fibrosis complicates the constrictive pericarditis. The most skillful resection may be to no avail if there is a diffuse fibrosis of the myocardium. 4. The fibrosis of the pleura or constrictive pleuritis has been a factor in causing postoperative disability in 50 per cent of his patients. 5. Changes in liver function may occur in long standing cases which may be irreversible even after a successful operation. 6. Persisting atrial fibrillation. 7. Etiological unrelated condition such as obesity, pregnancy, valvular disease, renal disease and chronic pulmonary disease may affect the outcome. 8. Hypertension which does not occur when there is marked disability from constrictive pericarditis developed in 3 of his patients after a successful operation.

Since the operation for constrictive pericarditis is in general not a curative procedure but a modifying one he concludes that it is obvious that a knowledge of these various complicating factors is essential for effective management in the years following operation.

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ELECTROCARDIOGRAM OF THE MONTH

The authors would be pleased to receive comment and controversy from readers in relation to explanations offered.

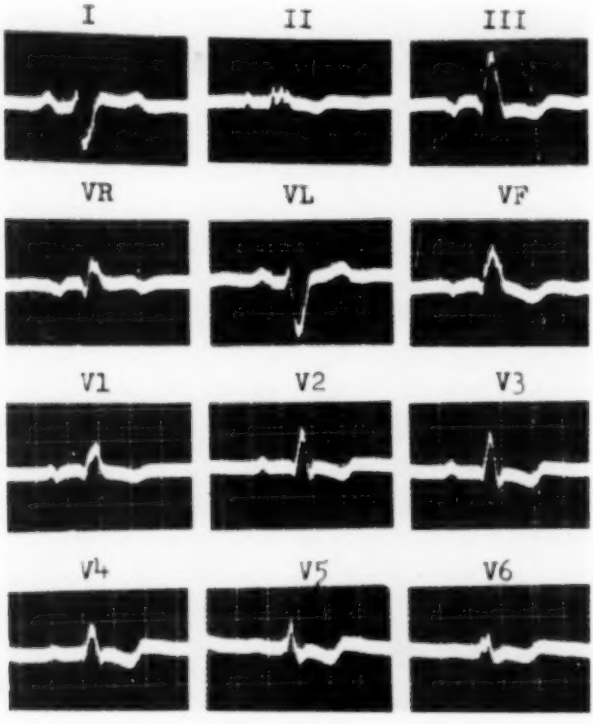
The Importance of the Unipolar Morphologies in Right Bundle Branch Block

Our usual approach to the electrocardiographic interpretation at the Department of Electrocardiography of the Instituto Nacional (Mexico City) is based on knowing only the age and sex of the patient and the presence or absence of cyanosis.

We try to suggest the diagnosis of the patient through the reading of the electrocardiogram and only after this step the clinical data are obtained in order to ratify or rectify our own diagnosis.

With the above in mind, we will start the interpretation of the tracing of a 26-year-old man without cyanosis:

Sinus rhythm. Average rate (determined before mounting this tracing): 75/min. P-R interval: 0.21-0.22 sec. in Lead I. First degree A-V block. QRS: 0.17 Sec. in Lead III. ∠QRS: around +135°. S∠QRS points to the front, right and downwards. ∠P: around −15°. The duration of the P wave in Lead I reaches 0.12 Sec. The P wave in V1 is diphasic, of the ± type, with a relatively slow inscription of its intrinsicoid deflection. Complete right bundle branch block. The QRS complex shows delayed intrinsicoid deflection in all the precordial leads. In this respect, we have to comment that some authors could erroneously speak



of bilateral bundle branch block; but if we carefully study all the unipolar morphologies in the precordial leads, we definitely arrive at the diagnosis of right bundle branch block. The morphology registered in V1 is of the qR type with a negative T wave; in V2 and V3 the complexes are of the qRs type, also with a negative T wave. We have described these morphologies as corresponding to the potential variations (not to be mistaken with action potential) of the right atrium or of very high portions of the free right ventricular wall near the anterior A-V groove. The complexes from V4 through V6 are of the Rs type with a negative T wave corresponding to potential variations of the free right ventricular wall and very probably those of V6 to the right lower septal mass. In other words, we are exploring through the precordial leads regions proximal to the right atrium and right ventricle. The left ventricle is explored only in aVL and in Lead I, where the morphology of the ventricular complex is of the rS type, with early inscription of the intrinsicoid deflection and a positive T wave.

With the above description the tracing is suggestive of:

1. Left atrial enlargement; based on the increased duration of the P wave in Lead I and the ĀP deviation to the left (to −15°).

2. Huge right atrium enlargement; based on the fact that we are recording the potential variations of this cardiac cavity from V1 through V3; the diphasic P wave of the ± type with slow inscription of its intrinsicoid deflection are in agreement with this diagnosis.

3. Right ventricular enlargement, since from V4 through V6 we are recording the potential variations of the right ventricle.

4. Marked clockwise rotation, since the right atrium and right ventricle occupy all the anterior aspect of the heart.

Taking into consideration the age of the patient three diagnostic possibilities are suggested:

a) Ebstein's disease

b) Rheumatic mitral-tricuspid disease

c) Lutembacher's syndrome.

The three clinical entities satisfactorily fit in with the electrocardiographic findings. After the study of the tracing and the mentioning of the above possibilities we revised the clinical chart and found that it was a case of rheumatic heart disease of the mitral-tricuspid type in congestive heart failure.

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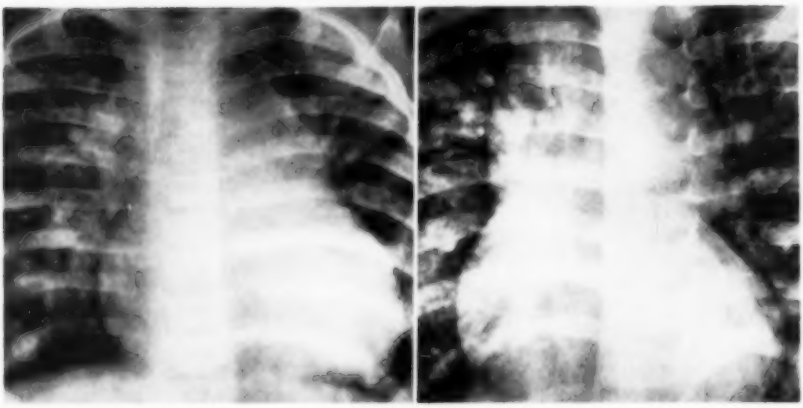

Figure 1A: Early film of angiocardiogram, showing dilatation of left innominate vein and superior vena cava.

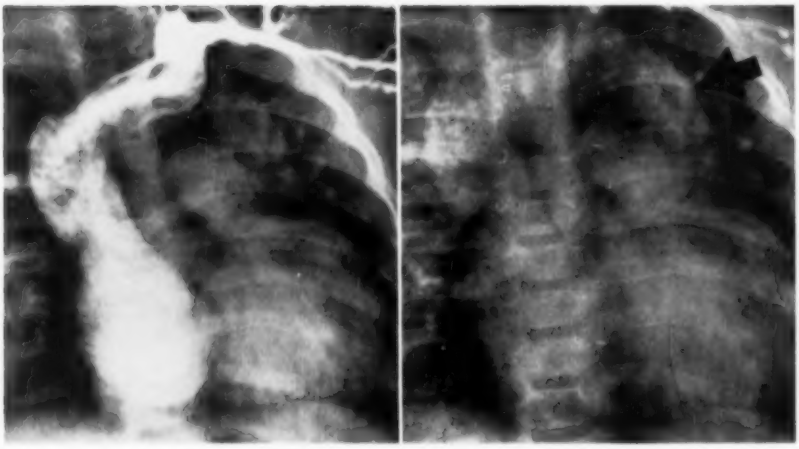

Figure 1B: Later film, showing opacification of the anomalous vertical pulmonary vein (arrow) draining into the left innominate.

Clinical Information

This white girl was first seen at the age of nine days with generalized mild cyanosis, present since birth. She was observed to have spells of rapid shallow respiration. No cardiac murmurs were detected at that time. The blood pressure was 110/80, the pulse 160, and the respirations 60. The liver edge was palpable just below the right costal margin. She was hospitalized again at the age of one year at which time she was still cyanotic and showed tachycardia. A systolic murmur was heard over the sternum.

The above chest film was made at the age of three. At that time she was still cyanotic. In addition to the earlier murmur, a diastolic murmur was now heard to the right of the sternum and posteriorly between the scapulae.

DIAGNOSIS

Anomalous Pulmonary Venous Return

These roentgenograms demonstrate the so-called figure-of-eight heart, which is considered diagnostic of anomalous pulmonary venous return. This condition is a congenital malformation in which one or more of the pulmonary veins empties into the right atrium or one of its tributaries, instead of into the left atrium. The figure-of-eight configuration occurs when most or all of the blood of one or both lungs drain into the right superior vena cava via an anomalous left vertical pulmonary vein emptying into the left innominate vein. The functional disturbance depends chiefly upon the details of the associated anomalies. The commonest of these is an atrial septal defect or a patent foramen ovale. When more than 50 per cent of the blood is shunted to the right side of the heart the outlook is grave. The most common clinical findings are dyspnea on exertion, mild cyanosis, and a loud systolic murmur to the left of the sternal border.

The chest film may be normal in the neonatal period, but the figure-of-eight deformity is seen in about half the cases before the age of three months. In addition to this configuration, the pulmonary arteries and their branches may be enlarged and considerable right atrial and right ventricular dilatation may be evident. The lower half of the figure-of-eight is formed by the heart, the left upper limb represents the anomalous vertical pulmonary vein, and the right upper limb the dilated superior vena cava resulting from the extra quantity of blood traversing it.

Angiocardiography (Fig. 1) confirms the diagnosis, and may demonstrate the associated anomalies.

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The Twenty-Year Course of Chronic Constrictive Pericarditis with Subsequent Surgery

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Chronic constrictive pericarditis is a disease characterized by gradual fibrosis, thickening and contraction of the pericardium and/or epicardium leading to a reduction of cardiac function. It is most frequently a complication of tuberculous pericarditis.

White reports[1] that chronic constrictive pericarditis was first described in 1669 by Lower. Burwell states[2] that since that time Lancisi, Morgagni, Laennec, Hope, Chevers and Pick have recognized and added additional information to further elucidate the pathophysiology.

In 1896, Weil and Delorme suggested[3] resection of the pericardium as a means of treating and perhaps curing chronic constrictive pericarditis. In 1920, Rehn[4] reported on the first successful operation. Churchill and White in 1929 reported[5] the first successful resection in this country.

There have only been a few reported cases of the disease followed from the initial infection to the constricting stage or to the time of operation. Furthermore some investigators report that surgical risk increases directly with the duration of the disease, the operative mortality high and the beneficial results dubious. In view of this, our paper is concerned with a patient with chronic constrictive pericarditis followed from the initial infection through 22 years of palliative management and the results obtained on this patient after pericardiectomy was performed.

M. C., a 47 year old colored woman entered the George W. Hubbard Hospital on November 30, 1956 complaining of shortness of breath, abdominal swelling and edema of the lower extremities. She had been followed in the cardiac clinic over a period of three years with similar symptoms. Numerous thoracenteses had been required to relieve her of dyspnea. Mercurial diuretics, diamox, a low sodium diet and other measures did not prevent her from becoming edematous and dyspneic to the point that she could not be managed on an outpatient basis.

A review of her history disclosed that 22 years ago on June 14, 1934 at the age of 24, she entered a local hospital complaining of chills, weakness, fatigue, muscular aches and pains. She had nausea, vomiting and severe diarrhea. These symptoms had existed for five weeks. There was weight loss of 22 pounds and cough productive of white frothy sputum. She denied hemoptysis. On examination her temperature was 103° F. She had tachycardia, and bilateral non-tender enlargement of the submaxillary and cervical lymph nodes. The area of cardiac dullness was enlarged to the left and right of the sternum. The heart sounds were distant and a pleuro-pericardial friction rub was heard along the left sternal border. The blood pressure was 130 mm. of Hg. systolic and 80 mm. of Hg. diastolic. A paradoxical pulse was present. There was dullness to percussion and diminished breath sounds in the left axilla. The remainder of the physical examination was not remarkable.

The hemogram revealed three million red blood cells and 6,450 white blood cells with a differential count of 60 per cent polymorphonuclear cells, 35 per cent lymphocytes, 3 per cent eosinophils, and 2 per cent basophils. Urine specific gravity 1.010, otherwise normal. The Wassermann and Kahn tests were reported as strongly positive. The venous pressure was 140-145 mm. of saline. X-ray film of the chest showed marked globular enlargement of the cardiac silhouette. There was no evidence of active pul-

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monary tuberculosis. Electrocardiogram revealed sinus tachycardia and first degree heart block. The tuberculin test was strongly positive in a 1:1000 dilution.

A diagnosis of acute pericarditis probably of tuberculous origin was made. After 34 days of non-specific therapy, she became afebrile and asymptomatic. She was discharged to be followed in the home. Approximately five months later she was readmitted to the hospital with a complaint of exertional dyspnea, headaches, and pain between the shoulders.

Physical examination on that admission revealed a moderately enlarged heart. There was dullness to percussion over the lower right lung posteriorly. The liver was palpable one and one-half fingersbreadth below the right costal margin. The venous pressure was 124 mm. of saline. A diagnosis of constrictive pericarditis was made. Surgery was advised but she refused. She was given symptomatic therapy and bedrest. After 10 days she was discharged again to the outpatient department. For a 10 year period extending from 1938 to 1948 she had no contact with the hospital and engaged in her occupation as a cook with only minimal disability.

During the latter half of 1948 she was seen at another local hospital for an abscess in the upper lateral area of the right thigh. Incision and drainage was performed but no bacteriological diagnosis was made. Three months later she developed an abscess in the same area of the left thigh and the tissue removed was described by the pathologist as being granulomatous. One year later she was treated at the George W. Hubbard Hospital for a chronic draining abscess of the right thigh. Tubercle bacilli were isolated from the exudate. In 1952 she developed a right psoas abscess that required incision and drainage.

In 1954, 20 years after the initial diagnosis of acute tuberculous pericarditis, she was admitted to the George W. Hubbard Hospital because of dyspnea, abdominal distension, and edema of the lower extremities. She had generalized cardiac enlargement, distant heart sounds, auricular fibrillation, pulmonary rales, ascites hepatomegaly, edema of the lower extremities and the venous pressure was increased. A diagnosis of constrictive pericarditis was made but she refused the suggested operation. She responded slightly to a low salt diet, digitalization and mercurial diuretics.

During the next two years she was hospitalized on numerous occasions due to the above symptoms. She developed right pleural effusion which required thoracenteses at monthly intervals. A total of (36 liters) of serous fluid was removed from the right pleural space during this period. It became more difficult to manage her and weekly thoracenteses were necessary just prior to the last admission. She was unable to perform any work and became dyspneic at bed rest. The ascites increased and edema of the lower extremities became more pronounced. Diuretics were ineffective. She appeared terminally ill and this hospitalization was recommended.

Examination at the present admission revealed her to be a well developed, poorly nourished middle aged markedly dyspneic woman. The blood pressure was 110/72, temperature 99.2° F., pulse 90 per minute and respirations were 24 per minute. There

FIGURE 1

FIGURE 2

Figure 1: Chest x-ray revealing pleural effusion prior to thoracic tap and surgery.—*Figure 2:* Chest x-ray two and one-half weeks post-operatively.

was marked distension of the neck veins. The area of cardiac dullness was moderately enlarged to the left. The heart sounds were faint and of poor quality. The heart rhythm was totally irregular. Tactile fremitus was decreased over the lower half of the posterior right lung and breath sounds were diminished in that area. There was dullness to percussion in the posterior aspect of the lower right lung field. Moist rales were present in the base of the left lung. The abdomen was protuberant and there was shifting dullness to percussion in the flanks. The abdominal wall was tense, shiny, and edematous. The liver was not palpable but there was percussion dullness extending to the umbilicus. There was 4+ pitting edema of the thighs, legs and feet.

Laboratory findings revealed a white blood cell count of 7,550 with a differential of 62 per cent polymorphonuclear cells, 35 per cent lymphocytes. The hemoglobin was 13.2 grams per cent and the hematocrit was 41 per cent. The pertinent urinary findings were specific gravity of 1.010 with 3-4 W.B.C. per high power field and an occasional granular cast. The blood chemistry studies were as follows: total serum protein 4 grams per cent, with albumin 2.6 grams per cent and globulin 1.4 grams per cent. The blood sugar was 94 mgm. per cent, and the N.P.N. was 25 mgm. per cent. The circulation time was 35 seconds and the venous pressure was 300 plus mm. of saline.

The pleural fluid appeared slightly serosanguineous with specific gravity of 1.012, two polymorphonuclear cells per cubic millimeter, 24,000 erythrocytes per cubic millimeter, and 0.3 grams per cent of proteins. X-ray film of the chest revealed moderate cardiac enlargement, slight enlargement of the pulmonary artery segment, slight aortic widening with elongation and minimal calcification, bilateral pulmonary congestion and pleural fluid in the right lung base. The electrocardiogram showed atrial fibrillation, low voltage on the QRS complexes, and diphasic to inverted T waves.

Therapy consisted of a low salt diet and maintenance digitalis. Thoracenteses were performed weekly. Diamox and mercuhydrin were used for diuresis. Even with this rigorous therapy the pleural fluid accumulated rapidly. The ascites also increased. She could not tolerate even minimal activity and was confined to bed. At this time she consented to surgical therapy.

The operation was performed on January 8, 1957, 22 years after the initial diagnosis was made. The heart was found encased in a thick fibrous pericardium which severely restricted its movements. The fibrous pericardium was removed from both ventricles. The myocardium appeared slightly atrophic, but a marked increase in cardiac pulsations could be seen after the removal of the constrictive tissue. She tolerated the procedure well. Five days postoperatively the venous pressure had fallen to 220 mm. of saline and the circulation time was 13.4 seconds. There was a marked increase in the urinary output up to 2,000 ml. a day without diuretics. The edema and ascites subsided. She improved progressively and one month after operation the venous pressure was 90 mm. of water and the circulation time was 15.8 seconds. The total serum proteins increased to 5.8 grams per cent. A liver profile revealed a negative cephalin flocculation test, a serum bilirubin of 0.7 mgm. per cent, a prothrombin time of 17.8 seconds with 69 per cent activity. The total cholesterol was 270 mgm. per cent and the cholesterol esters 171 mgm. per cent. She was up and about the ward without dyspnea and was discharged on February 9, 1957 to be followed in the cardiac clinic.

She has been followed in the clinic for 12 weeks postoperatively and has not required a thoracentesis since the immediate postoperative withdrawal of fluid. She shows gradual improvement and is well maintained with a low salt diet and mercurial diuretics. She is able to do minimal house work at this time and states she never realized how well she could feel.

DISCUSSION

The importance of making a correct diagnosis cannot be overstated. The recent development of antituberculous agents renders constrictive pericarditis, in a great many instances, among the preventable diseases. The rapid development in thoracic surgery has rendered the condition among the curable and, if not curable, symptoms can be greatly ameliorated and life prolonged.

The diagnosis may not always be as clear as in our patient. It may mimic heart disease with predominant right ventricle failure. The persistance of ascites, hepatomegaly and marked elevation of venous pressure with lack of response to therapy should give a clue to the possibility of constrictive pericarditis. The inability of the patient to increase her cardiac output upon activity is a significant clue. X-ray and E.K.G. changes are also of value in establishing the diagnosis.

The specific treatment of chronic constrictive pericarditis is an operation consisting of removal of the thickened pericardium. Burwell[6] states that the operation is in general not a curative procedure but a modifying one. This is due to the fact that the majority of patients still have some residual objective signs although they may have marked subjective improvement.

The primary purpose of an operation is the release of the two ventricles from the constricting pericardium. The improvement after operation is slow and may be incomplete. However, this fact should not deter physicians from recommending an operation in patients with constrictive pericarditis.

In the case presented, it was felt that after 22 years with constrictive pericarditis, the patient had become a poor surgical risk for the following reasons: 1) The possibility of myocardial fibrosis and atrophy suggested there may be little improvement after operation. 2) Chronic hepatic congestion may have led to irreparable liver damage such as cardiac cirrhosis. 3) The possibility of acute dilatation of the atrophic ventricular myocardium when the constricting scar was removed. However, the patient tolerated the operation well. After the pericardial scar was removed from the ventricles, the underlying myocardium did not appear too atrophic and an increase in contractions could be seen immediately.

After operation, the circulation time and venous pressure fell to near normal range. In spite of continued improvement, the patient still develops pleural fluid, some ascites and dependent edema. This however can be well controlled with diuretic drugs, and thoracenteses have not been necessary 12 weeks post-operatively. This would indicate that in spite of the duration of the disease, if a diagnosis of constrictive pericarditis is made, the patient should be given the benefit of surgery.

Special acknowledgment is given to Dr. John Thomas for his kind assistance in the preparation of this paper.

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Editorial

Radiation Hazards

The American College of Radiology and the American College of Chest Physicians have a joint committee on chest x-ray which has been meeting annually for the past eight years. At the last meeting of this joint committee, the results of a questionnaire mailed to members of the American College of Chest Physicians concerning the use and present status of their x-ray and fluoroscopic equipment, were analyzed and discussed. It was the opinion of the joint committee that some simple rules concerning the use of this equipment in our offices and hospitals should be enumerated.

One can improve the status of the apparatus in our individual offices or in the apparatus we might control elsewhere, by obtaining the "Practical Manual on Medical and Dental Use of X-rays with Control of Radiation Hazards" prepared by the American College of Radiology and recently made available to all physicians. Do not neglect to save and study your copy. It emphasizes the necessity for perspective and common sense in our approach to the problem of protection to both the patient and the operator of the fluoroscopic and radiographic apparatus.

We should periodically check the output of the machine and have it tested for stray radiation. Check on the proper filtration of the primary beam of radiation.

When fluoroscoping, be sure to dark-adapt for at least ten minutes in order to be able to use the least possible time of exposure to the patient and operator.

Use the lowest radiation output possible, remembering that any radiation one gets unnecessarily is too much. For additional protection to the operator, use the shortest time possible and use protective gloves and apron.

For further protection to the patient, use the smallest shutter opening when fluoroscoping, and keep the primary beam away from the gonads. Have films made for doubtful findings rather take the chance of overexposure by long continued fluoroscopy. Radiography requires less dosage. Use special care with infants, children, the pregnant mother and the potentially pregnant woman.

Always ask the question of yourself, "Is this examination necessary? Is the need for the procedure greater than the hazard, small though it might be?"

The membership can get further detailed information in the Handbooks No. 59 and No. 60 of the National Committee on Radiation Protection. These are for sale by the Superintendent of Documents, Washington 25, D.C. at 30 cents and 20 cents respectively.

If we put into practice these relatively simple means of protection, we are then using the common sense approach which has been urged to prevent unnecessary fear and misunderstanding on the part of the laity. We can then correct any misinterpretation and answer the patients' questions with confidence.

PAUL C. SWENSON, M.D., F.C.C.P.
St. Paul, Minnesota

College Chapter News

California Chapter

The annual meeting of the California Chapter will be held at the Sheraton-Palace Hotel, San Francisco, February 21. The following program will be presented:

9:00 a.m. Registration

9:15 a.m. Introductory Remarks: Elmer Rigby, Los Angeles, President

9:30 a.m. Scientific Session—Elmer Rigby, moderator
"Chemotherapeutic Aspects of Pulmonary Tuberculosis"
James A. Wier, Denver, Colorado
Discussion: Emil Bogen, Olive View
"Rational Vasopressor Treatment of Cardiac Arrhythmias"
Eliot Corday, Beverly Hills
"Value of Serum Enzymes in the Diagnosis of Myocardial Infarction"
John Sampson, San Francisco
"Pneumoperitoneum—Past and Present"
C. Gerald Scarborough, San Jose
Panel Discussion—"What We Think about Pneumoperitoneum"
Panel: J. Lloyd Eaton, Oakland; A. Gerson Hollander, Oakland; William Leftwich, Oakland; Robert Quinn, Santa Rosa

12:00 noon Luncheon

2:00 p.m. X-ray Panel Discussion
Moderator: James E. Kieran, Oakland
Panel: Lyman A. Brewer, III, Los Angeles; William Farraghan, Oakland; L. Henry Garland, San Francisco; A. Gerson Hollander, Oakland; James A. Wier, Denver

3:00 p.m. Scientific Session—David J. Dugan, Oakland, Moderator
"Groundwork in the Establishment of a Thoracic Surgical Section"
J. Gordon Strance, Napa
"Tuberculin Skin Testing: A Report"
J. Hallam Cope, Oakland
"Confessions of an Honest Chest Surgeon"
Robert Jamplis, Palo Alto
Discussion: Donald Rowles, Palo Alto
"Management of Coccidioidal Cavitation in an Endemic Area"
Byron Evans, Fresno
Discussion: William A. Winn, Springville

Hong Kong and China Chapter

The annual meeting of the Hong Kong and China Chapter was held on November 28 at the Hong Kong Sanatorium and Hospital. Sister Mary Aquinas, Chapter President, presided and gave a resume of the post-congress meeting held in september in Hong Kong. Dr. Stephen D. Sturton, Secretary, reported on the 7th International Cancer Congress held in London. The following officers were elected:

President	Stephen D. Sturton, Hong Kong
Vice President	Hee-Chee Chan, Hong Kong
Secretary-Treasurer	Phyllis Haddow, Hong Kong

New England States Chapter

The following officers were elected at the annual meeting of the New England States Chapter on December 10 at the University Club, Boston:

President	Maurice S. Segal, Boston (re-elected)
1st Vice President	Joseph N. Corsello, Providence, R.I. (re-elected)
2nd Vice President	Max G. Carter, New Haven, Connecticut
Secretary-Treasurer	S. Clive Cohen, Boston (re-elected)

The next all-day scientific meeting of the chapter will be held in Boston on April 4.

Obituaries

DARCY R. W. COWAN

1885-1958

Sir Darcy Cowan, Governor of the College for South Australia, died at the age of 72 on June 8 in Adelaide after a long illness. Sir Darcy, widely known for his outstanding work in the care and treatment of tuberculosis, was medical director of the South Australia Tuberculosis Association and Honorary Secretary of the National Association for the Prevention of Tuberculosis in Australia. He was the founder of both of these organizations as well as the Australian Laennec Society which, for the first time this year, will give the Cowan Prize to perpetuate his name. In recognition of his ceaseless efforts for tuberculosis sufferers, the main building at Bedford Industries, a rehabilitation center for tuberculosis patients, was named for him. Sir Darcy Cowan was credited as the principal instigator in the establishment of this center and served as medical director and member of the board of management. In addition, he was the founder and first president of the Northcote Home, a home for the children of tuberculous mothers. In 1955 he was knighted in recognition of his many contributions in the field of tuberculosis.

Born at Norwood, Sir Darcy Cowan was educated at Prince Alfred College and the University of Adelaide where he later served as lecturer on pulmonary tuberculosis. In 1935-36 he was President of the South Australia branch of the British Medical Association.

In addition to his scientific activities, Sir Darcy Cowan was well known in the field of sports. He was one of the University of Adelaide's few triple blues, having won them for lacrosse, football and tennis. He was an honorary life member of the South Australia Lawn Tennis Association of which he was vice-president for twenty-three years until his resignation last year.

Sir Darcy Cowan was elected to Fellowship in the College in 1946 and his interest in College affairs led to his appointment as Governor in 1947. His passing is a great loss, not only to the College and his many friends, but to the entire medical profession.

W. Cotter Harvey, M.D.
Regent for Australia

HENRY BOSWELL

1884-1957

Dr. Henry Boswell, age 73, passed away at the Mississippi State Sanatorium on December 16, 1957, after an illness of several months. He had been the superintendent and guiding spirit of the sanatorium for 40 years, having assumed his duties there on August 4, 1917. Under his direction, the sanatorium became one of the outstanding institutions of its kind and he was nationally known for his work.

Dr. Boswell was past president of the Mississippi State Medical Association, the Southwest Medical Association and the American Trudeau Society. He was chairman of the Mississippi Commission on Hospital Care and a member of the Board of Trustees of Mental Institutions. He was a member of the Central Medical Society, Mississippi State Medical Association, Southern Medical Association, American Medical Association, Fellow of the American College of Physicians and Fellow of the American College of Chest Physicians.

A member of the faculty of the University of Mississippi for many years, he was instrumental in obtaining a 4-year medical school for Mississippi.

More important to him than those honors was his place in the hearts of his fellow man, all races and creeds. He always sought ways to be a help to others and there was no man so mean that his friendship was not valued by Henry Boswell.

He is survived by his widow, Mrs. Iola Saunders Boswell, one son, Col. Henry Boswell, Jr., United States Army, 4 daughters, Mrs. Howard Dear, Mrs. William L. Tyson, Jr., Mrs. Karl Stauss, Mrs. Samuel B. Johnson, all of Jackson, Mississippi, one brother, three sisters and fifteen grandchildren.

Clyde A. Watkins, M.D.

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Physician wanted interested in pulmonary diseases for 170-bed state supported tuberculosis hospital established 3 years. Active surgical program, outpatient service, x-ray and laboratory. Consultants in all branches. U. S. citizenship and Alabama medical license or eligibility therefor required. Salary $8500 to $9500 depending on qualifications. Quarters to be made available. Apply: Medical Director, Sixth District Tuberculosis Hosptial, 800 St. Anthony Street, Mobile, Alabama.

Vacancy—medical staff. Permanent appointment available. Annual salary range: $7284-$9466, plus personal and/or family maintenance. Write: Superintendent, Essex Sanatorium, Middleton, Massachusetts.

CALENDAR OF EVENTS

National Meetings

Twenty-fifth Annual Meeting
Silver Anniversary, American College of Chest Physicians
Ambassador Hotel, Atlantic City, New Jersey
June 3-7, 1959

Homecoming Meeting
Silver Anniversary, American College of Chest Physicians
Albuquerque, New Mexico, October 14-17, 1959

Postgraduate Courses

4th Annual Course on Diseases of the Chest
San Francisco, California, February 16-20, 1959

12th Annual Course on Diseases of the Chest
Philadelphia, March 30-April 3, 1959

4th Regional Course on Diseases of the Chest
Newark, New Jersey, April 1, 8, 15, 22, 1959

Chapter Meetings

California Chapter, San Francisco, February 21, 1959
New York State Chapter, New York City, March 19-20, 1959

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SILVER ANNIVERSARY MEETING

HOTEL RESERVATION FORM

25th Annual Meeting
AMERICAN COLLEGE
OF
CHEST PHYSICIANS

Ambassador Hotel
Atlantic City, New Jersey

June 3-7, 1959

108th Annual Meeting, American Medical Association
Atlantic City, New Jersey, June 8-12, 1959

The Ambassador Hotel, Atlantic City, will be headquarters for the 25th Annual Meeting of the American College of Chest Physicians. Members planning to attend the meeting are urged to make their reservations at once, in order to obtain accommodations at the College headquarters hotel. Please use this convenient order form and mail directly to the Ambassador Hotel.

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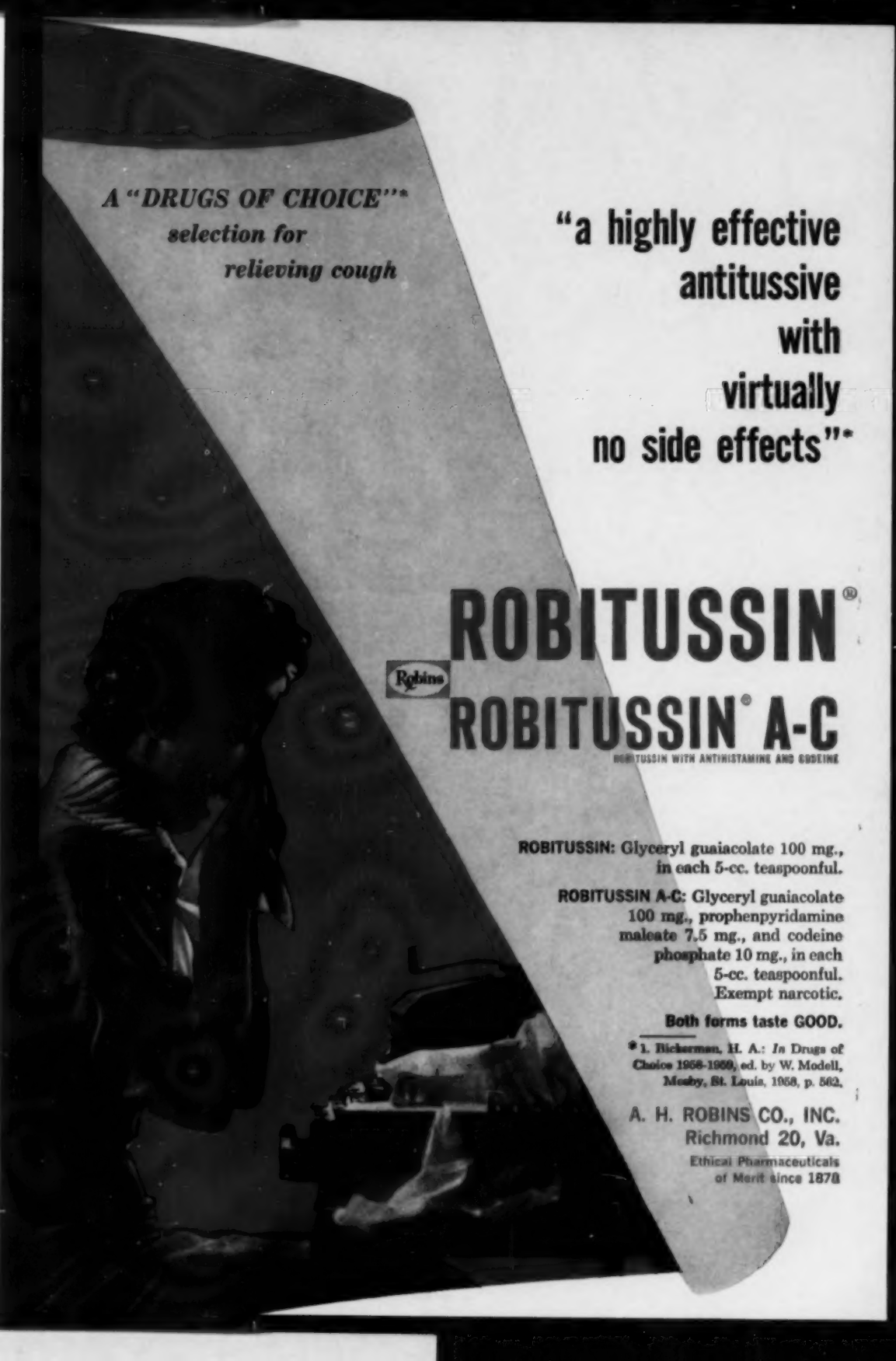
Remarks _____



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* 1. Bickerman, H. A.: *In* Drugs of Choice 1958-1959, ed. by W. Modell, Mosby, St. Louis, 1958, p. 562.

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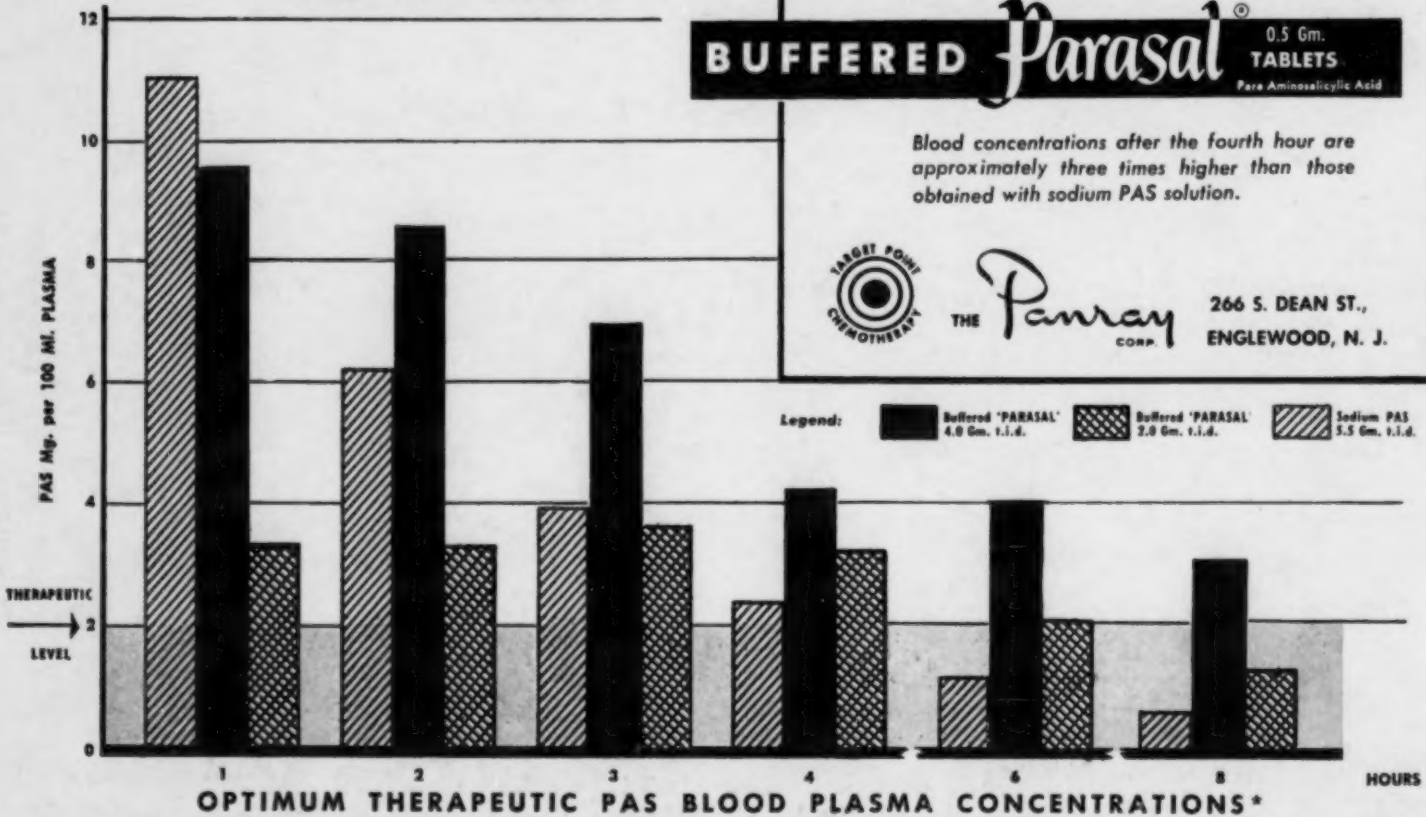

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Ref.: Deeb, E. N. & Vitagliano, G.R.: A. Rev. Tuber. & Pul. Dis.: 72,543-7 (Oct. '55)

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